Disclosure of HIV status among HIV-infected pregnant and postpartum women in Cape Town, South Africa

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Abstract

Background: With 2.7 million women living with HIV, the burden of HIV remains high in South Africa but adherence to antiretroviral therapy remains a concern among pregnant and postpartum women. Disclosure, or the process of gradually revealing one's HIV status to individuals in one's social network, is regarded as an important factor in HIV care, with potential benefits that include improved psychological well-being and adherence to antiretroviral therapy. This thesis sought to provide insights into the patterns, predictors and impact of HIV-status disclosure among pregnant and postpartum women in the context of lifelong antiretroviral therapy in South Africa, including considerations of stigma, social support, depression and unintended pregnancy.

Methods: This research included women living with HIV in Gugulethu, Cape Town. A total of 1554 pregnant women were enrolled; those who were initiating antiretroviral therapy were followed up to 18 months postpartum, with one further visit at 36-60 months postpartum. Data were collected using questionnaires and blood specimens for HIV viral load testing.

Findings: Across analyses, women's social and economic circumstances emerged as central to understandings of disclosure, mental health and viral load. At entry into antenatal care, 95% of women who were diagnosed HIV-positive before the pregnancy had disclosed to at least one person but disclosure events formed two separate dimensions: disclosure to (i) a male partner and (ii) family/community members. Among women diagnosed during the pregnancy and initiating antiretroviral therapy, 61% disclosed to a male partner and 71% to a family/community member by 12 months after diagnosis; relationship status modified the impact of each of pregnancy intentions and poverty on disclosure to a male partner.

During pregnancy, 1 in 10 women reported elevated depressive symptoms and 60% of women who were subsequently followed during the postpartum period reported that their pregnancy was unintended. Stigma modified the association between social support and depression: when levels of stigma were high, higher levels of social support were not associated with decreased depressive symptoms. Pregnancy intention modified the impact of disclosure to a male partner on depression during pregnancy: disclosure was associated with higher depression scores among women who reported that their current pregnancy was unintended but was associated with lower depression scores among women who reported that the pregnancy was intended. Further, unintended pregnancy was a persistent predictor of elevated viral load up to 60 months postpartum.

Finally, the effect of disclosure on elevated viral load at entry into antenatal care, delivery and 12 months postpartum was complex and modified by three factors: (i) timing of HIV diagnosis (before versus during the pregnancy); (ii) relationship to the person(s) to whom women disclose; and (iii) in the case of disclosure to a male partner, relationship status.

Conclusions: These findings suggest that despite the widely-held view that disclosure has beneficial impacts on psychological well-being and adherence, the individual is central to our understanding of disclosure. In particular, both the prevalence of disclosure and its impact on depression and viral load are modified by women's circumstances. Unintended pregnancy emerged as a critical factor that heightens women's vulnerability. In this setting, HIV-status disclosure does not appear to be universally beneficial and counselling about disclosure may be most effective if tailored to individual women's circumstances.

Declarations

This thesis is presented in fulfilment of the requirements for the degree of Doctor of Philosophy (PhD) in the School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town.

The work included in this thesis is original research and has not, in whole or in part, been submitted for another degree at this or any other university. The contents of this thesis are entirely my own work or, in the case of multi-authored papers, constitutes work for which I was the lead author. My contribution to multi-authored papers is outlined at the beginning of each results chapter.

I confirm that I have been granted permission by the University of Cape Town's Doctoral Degrees Board to include the following publications in my PhD thesis, and where co-authorships are involved, my co-authors have agreed that I may include the publications:

1. Brittain K, Mellins CA, Remien RH, Phillips T, Zerbe A, Abrams EJ, Myer L. Patterns and predictors of HIV-status disclosure among pregnant women in South Africa: dimensions of disclosure and influence of social and economic circumstances. AIDS Behav. 2018;22(12):3933-3944.
2. Brittain K, Mellins CA, Phillips T, Zerbe A, Abrams EJ, Myer L, Remien RH. Social support, stigma and antenatal depression among HIV-infected pregnant women in South Africa. AIDS Behav. 2017;21(1):274-282.
3. Brittain K, Mellins CA, Remien RH, Phillips T, Zerbe A, Abrams EJ, Myer L. HIV-status disclosure and depression in the context of unintended pregnancy among South African women. Glob Public Health. 2019;14(8):1087-1097.
4. Brittain K, Phillips TK, Zerbe A, Abrams EJ, Myer L. Long-term effects of unintended pregnancy on antiretroviral therapy outcomes among South African women living with HIV. AIDS. 2019;33:885-893.
5. Brittain K, Mellins CA, Remien RH, Phillips T, Zerbe A, Abrams EJ, Myer L. Impact of HIV-status disclosure on HIV viral load during pregnancy and postpartum in Cape Town, South Africa. J Acquir Immune Defic Syndr. 2019;81:379-386.

At the time of examination, not all publications were in their final published form. The versions submitted for examination are included here. Per University guidelines, the text of each paper is presented verbatim in this thesis. As such, there are minor discrepancies in terminology between papers; these have not been changed in order to reflect the publications. Minor changes have been made to style and to figure and table numbers to ensure consistency throughout this thesis.

Signed by candidate

Kirsty Brittain

October 2019

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List of Abbreviations

aHR	adjusted hazard ratio
aOR	adjusted odds ratio
aRR	adjusted risk ratio
ART	antiretroviral therapy
AUDIT	Alcohol Use Disorders Identification Test
AUDIT-C	Alcohol Use Disorders Identification Test – Consumption
AZT	zidovudine
CI	confidence interval
EPDS	Edinburgh Postnatal Depression Scale
HR	hazard ratio
IQR	inter-quartile range
LMIC	low- and middle-income country
LMUP	London Measure of Unplanned Pregnancy
m	months
MCH-ART	Maternal and Child Health – Antiretroviral Therapy
MOU	Midwife Obstetric Unit
MTCT	mother-to-child transmission
NHLS	National Health Laboratory Services
NVP	nevirapine
OR	odds ratio
PMTCT	prevention of mother-to-child transmission
RR	risk ratio
SD	standard deviation
SE	standard error
VL	viral load

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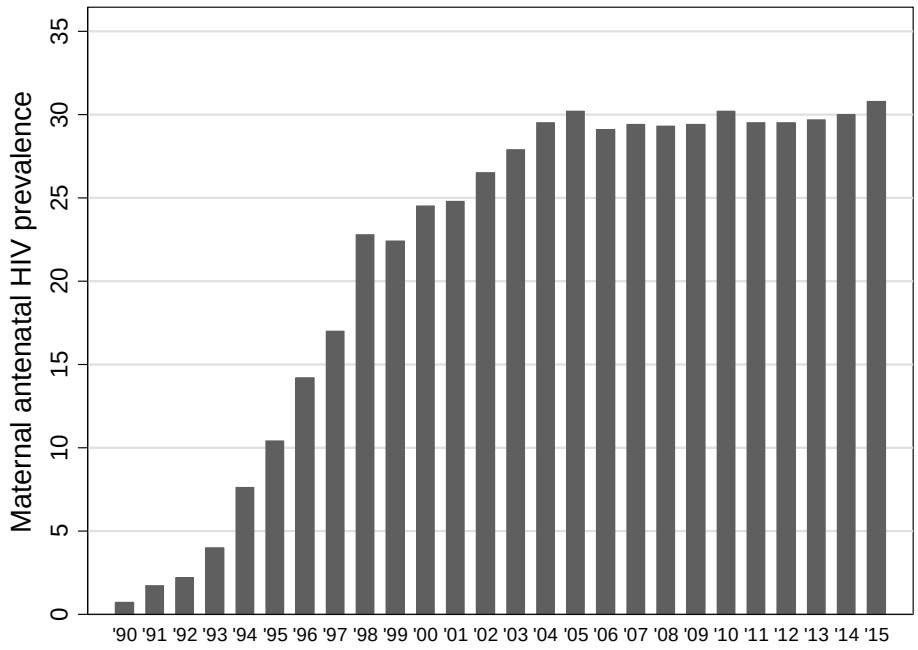
Chapter 1: Introduction

1.1 Introduction and Background

1.1.1 Background

Globally, more than 18 million women aged 15 years and older were living with HIV in 2017, including 2.7 million women in South Africa [1]. With the largest epidemic in the world, the burden of HIV in the country remains high, including among pregnant women. Surveillance data suggest that the maternal antenatal HIV prevalence in the country increased dramatically from 1990 (Figure 1.1), stabilising at around 30% [2]. Alongside global increases in the prevalence of HIV among general adult populations and among pregnant women, concerns arose regarding HIV-status disclosure, particularly to sexual partners, in order to reduce transmission and ensure support for HIV-infected individuals. Indeed, early guidelines for the management of HIV during pregnancy included the recommendation that all women be encouraged to disclose, or reveal their HIV status, to their partner [3].

Figure 1.1 Maternal antenatal HIV prevalence between 1990-2015 in South Africa [2]



In the absence of any preventive measures, the risk of mother-to-child transmission (MTCT) of HIV reaches 45% [4], but massive progress in prevention has been made globally. In South Africa, guidelines for the prevention of mother-to-child transmission (PMTCT) have evolved considerably since initial implementation during 2002. Table 1.1 presents an overview of changes in the maternal components of PMTCT guidelines in South Africa [5]. These have evolved from the provision of single-dose nevirapine (NVP) during labour, to all pregnant and breastfeeding women being eligible to initiate lifelong antiretroviral therapy (ART) under the World Health Organization's 'Option B+' approach. This approach was piloted at several sites in South Africa from 2013-2014 and was rolled out nationally in 2015. Alongside immediate initiation of lifelong ART, PMTCT guidelines in the Western Cape province in South Africa recommend that all HIV-infected women receive support for disclosure [6]. Disclosure is promoted as having both population- and individual-level benefits, as discussed under Section 1.1.3, below.

Table 1.1 Evolution of maternal components of prevention of mother-to-child transmission (PMTCT) guidelines in South Africa [5]

Year	Maternal PMTCT components[1]
2002	Single-dose NVP given to mothers during labour
2004	AZT given to mothers from 28 weeks gestation and single-dose NVP given during labour
2010	AZT given to mothers from 14 weeks gestation
2013	All pregnant women eligible for ART, but women with CD4 cell count >350 cells/mm^3 and no other indication for ART to stop ART after the end of breastfeeding
2015	All pregnant and breastfeeding women eligible for lifelong ART

[1] NVP: nevirapine; AZT: zidovudine; ART: antiretroviral therapy

The provision of antiretroviral treatment is one aspect of the World Health Organization's four-pronged approach to prevent MTCT, embedded in which is the promotion of disclosure [7]. These four components include: (i) among women of childbearing age, preventing new HIV infections; (ii) among HIV-infected women, preventing unintended pregnancies and (iii)

preventing HIV transmission to their infants; and (iv) providing treatment, care and support to HIV-infected women as well as their children and families [7]. Among both pregnant women and general adult populations, HIV care occurs across a cascade, from HIV testing and linkage to HIV care, to sustained engagement in care and adherence to ART. The final stage of the maternal treatment cascade is HIV viral suppression, or undetectable viral load, which is critical to promoting health, slowing disease progression, and reducing the risk of onward transmission of HIV. Although viral suppression can be compromised by factors such as drug resistance, the strongest predictor of viral suppression is adherence to ART [8]. Indeed, adherence is the behavioural mechanism of viral suppression, and the success of ART is primarily determined by adherence [9]. As such, HIV viral load is used in both research and practice as an objective marker of adherence [8].

1.1.2 ART adherence during pregnancy and postpartum

With preventive measures and sustained viral suppression, MTCT rates close to zero have been documented [10]. In South Africa, high coverage of PMTCT programmes has led to dramatic reductions in MTCT [11]. During 2010, the incidence of MTCT at 6 weeks postpartum was around 3.5% [12] and decreased to around 1.5% in 2015 [13]. However, women's adherence to ART during the postpartum period is a major concern in South Africa and globally [14-16]. Further, in South Africa and many similar settings HIV care is integrated into antenatal care during pregnancy, but women must transfer to general adult ART clinics immediately post-delivery, and this transition may reflect a particularly risky period [17, 18], with implications for women's retention in care during the postpartum period. A recent systematic review of studies reporting data on retention in Option B+ programmes in Africa reported that retention ranged from 47-88% in the 6 months after ART

initiation; pooled estimates suggest that only 76% of women were retained in care 12 months after ART initiation [19].

Among general adult populations, psychosocial barriers to ART adherence may have profound effects on adherence [20]. Among pregnant and postpartum women, barriers may be even more pronounced as women must quickly adjust to a pregnancy and related demands and responsibilities; breastfeeding and infant care after delivery; as well as a new HIV diagnosis and starting lifelong ART for women diagnosed during the pregnancy or newly eligible to initiate ART [21]. At the same time, the timely initiation of ART and maintaining high levels of adherence is imperative for both maternal and child health outcomes. While improvements in ART availability and changing treatment guidelines have led to massive progress in reducing MTCT, pregnant and postpartum women represent a particularly vulnerable group for poor treatment outcomes, and there is an urgent need to understand how factors in these women's lives affect their likelihood of being retained in care and remaining adherent to ART [21]. Chapter 2 presents a conceptual framework reflecting determinants of ART adherence in the context of PMTCT, including the major constructs of interest on which this thesis focusses.

1.1.3 Potential benefits of HIV-status disclosure

A widely-cited barrier to achieving optimal treatment outcomes is limited disclosure of one's HIV status [21-24]. Indeed, major barriers to women's retention in Option B+ programmes in Africa include women's fears of inadvertent disclosure or reactions to HIV-status disclosure [19]. Disclosure has been defined as the gradual, sequential process of revealing one's HIV status to an increasing number of individuals over time [25, 26]. The conceptual underpinning of this thesis is the Disclosure Processes Model, which has been posited as a

framework to understand when and why disclosure is beneficial [27, 28]. This framework is presented and discussed in Chapter 2.

As alluded to above, disclosure is promoted as having both population- and individual-level benefits. At the population level, potential benefits include decreases in the incidence of HIV through behavioural change to reduce the risk of horizontal transmission. As such, there has been much focus historically on disclosure to sexual partners, and on promoting disclosure within sexual partnerships. Indeed, disclosure of an HIV-positive status is mandated in certain settings, with transmission criminalised [29]. Even in the absence of criminalisation, however, disclosure is seen as imperative to risk reduction and consequent reduction of the incidence of HIV [26]. Among pregnant and postpartum women, the prevention benefits may be two-fold: reduced transmission to HIV-uninfected sexual partners and reduced transmission to infants. At the individual level, disclosure is widely regarded as being an important factor in HIV care by potentially improving psychological well-being, ART adherence and treatment outcomes. Benefits to psychological well-being are thought to result from increased social support following disclosure [30]. Conversely, limited disclosure to individuals within the home or support network has been identified as a barrier to adherence in general HIV [20] and PMTCT programmes [31] through mechanisms which include not receiving support for adherence and secrecy around ART use.

1.1.4 Disclosure as a public health issue

Given these potential population- and individual-level benefits, HIV-status disclosure is strongly promoted in policy as well as counselling messaging [29, 32]. As stated above, early guidelines for the management of HIV in pregnant women stated that all women should be encouraged to disclose to their partner [3], and HIV treatment guidelines in the Western Cape

include support for disclosure to supportive family members or friends as a strategy to promote adherence [6]. Further, these guidelines state that patients experiencing issues with non-disclosure or stigma should receive on-going counselling [6]. In line with this, community health workers are described in the World Health Organization's four-pronged approach to prevent MTCT as playing an important role in improving the uptake of PMTCT services, one aspect of which includes encouraging disclosure [7]. Along with other public health approaches, the above guidelines provide blanket recommendations that are not tailored to individual women's experiences; rather, they take the position that disclosure is universally beneficial, and thus that all women *should* disclose. The majority of research to date has echoed this viewpoint by exploring associations between disclosure and improved outcomes in total samples, assuming that the potentially beneficial effects of disclosure do not differ across individuals [28].

Alongside the viewpoint that disclosure is universally beneficial, there has been little consideration of the possibility that the benefits of disclosure may be dependent on women's relationships with the person(s) to whom they disclose [28]. Indeed, the Western Cape guidelines referred to above recommend disclosure to 'supportive family members or friends' without distinguishing between these [6]. Most research has similarly neglected to distinguish between relationships when exploring the prevalence of disclosure or the benefits thereof: the majority focusses on disclosure to any versus no persons [33]. This approach treats disclosure as a unidimensional process in which there is no difference between disclosing to, for example, a partner, sister or friend. A further limitation is the reliance on cross-sectional research to explore patterns and benefits of disclosure, despite disclosure being inherently a process that occurs over time [25]. This approach assumes that the benefits of disclosure are consistent over time. Taken together, limitations of research and practice to date include the

assumptions that (i) disclosure is universally beneficial with (ii) effects that are consistent over time, and (iii) that these benefits are consistent across the person(s) to whom individuals disclose. This thesis aims to quantitatively explore each of these assumptions, as described under Section 1.2, below.

1.1.5 Interrelated psychosocial factors

A factor that is closely interrelated with disclosure is HIV-related stigma. Given improved availability of and access to ART, HIV is now a chronic, manageable disease. However, it remains highly stigmatised; is transmissible; and requires lifelong adherence to ART. As such, an HIV-positive diagnosis has major implications for psychological well-being. Worldwide, disclosure is strongly encouraged for the reasons discussed above, but stigma remains pervasive in many settings and has detrimental effects on health and well-being. In addition, stigma constitutes a major barrier to disclosure in both general adult populations [34] and in the context of PMTCT [35], and stigma and discrimination may compromise women's retention in Option B+ programmes [19]. Chapter 2 includes a discussion of the conceptual framework related to stigma on which this thesis draws, and further elucidates the links between disclosure, stigma and HIV treatment outcomes.

A second factor that is closely related to disclosure and to stigma is social support. Support is a critical facilitator of adherence and psychological well-being, and the potential for enhanced support is cited as a major reason to disclose. In addition, low levels of support are commonly reported as being associated with high levels of stigma [34]. Third, disclosure may lead to improved mental health [36]. Common mental disorders such as depression are major barriers to ART adherence and HIV treatment outcomes [20, 24], lending further support for the promotion of disclosure. Taken together, each of HIV-related stigma, social support and

mental health are important factors that are closely linked to HIV-status disclosure as well as health and well-being and should be considered in disclosure research and practice.

1.1.6 Unintended pregnancy

Among HIV-infected pregnant women, an important but understudied issue is that of unintended pregnancy. Preventing unintended pregnancies is the second prong in the World Health Organization's approach to PMTCT [7], but the prevalence of unintended pregnancy remains high among women globally [37]. Ample qualitative research has described the profound implications of an unintended pregnancy for women's psychological well-being [38, 39]. Indeed, an unintended pregnancy and new HIV diagnosis during pregnancy may have major implications for disclosure to a male partner [38]. In South Africa, levels of unintended pregnancy are high [40, 41] and around 50% of HIV-infected women initiating ART during pregnancy are newly-diagnosed when entering antenatal care [42]. However, there has been little quantitative consideration of the links between unintended pregnancy and disclosure and of the impact of an unintended pregnancy on HIV treatment outcomes. As discussed above, disclosure is promoted as a universally beneficial act, including among pregnant women, and the potential for an unintended pregnancy to confer additional vulnerability is absent from practice. In addition, despite policy objectives promoting the integration of contraceptive and fertility planning services into other health services in South Africa [43], family planning is not routinely integrated into HIV care in the country.

1.2 Rationale

Taken together, HIV-status disclosure, the closely related constructs of HIV-related stigma and social support, poor mental health and unintended pregnancy may be important factors in PMTCT care. However, existing quantitative research has important limitations, which are

alluded to above and are described further in the literature review presented in Chapter 2. Given these limitations, additional high-quality evidence for the impact of these factors in the context of PMTCT is needed. In particular, empirical evidence testing the assumptions that (i) disclosure is universally beneficial with (ii) effects that are consistent over time, and (iii) that these benefits are consistent across the person(s) to whom individuals disclose is needed to inform both research and practice. As argued above, factors such as stigma, social support, mental health and unintended pregnancy must be considered in explorations of disclosure and the potential benefits thereof. Given the relatively recent adoption of Option B+ guidelines and the consequent increasing numbers of women initiating lifelong ART during pregnancy, explorations of the factors which compromise high levels of adherence and viral suppression in this population are needed to reduce HIV transmission and promote maternal and child health within this vulnerable and growing population.

As described above, HIV care exists along a continuum. This thesis focusses specifically on the final step in the maternal treatment cascade: HIV viral suppression. Although retention in care and adherence to ART are critical steps in this cascade, this thesis takes the viewpoint that these outcomes are behavioural mechanisms of viral load and focusses on viral suppression as the ultimate goal of ART use for prevention and treatment. Thus, when examining the effect of disclosure on viral load, retention in care and adherence to ART are assumed to be the behavioural mechanisms of any possible associations: the assumption is that disclosure facilitates engagement in care and optimal adherence to ART which result in sustained viral suppression. Further, measuring each of retention and adherence is difficult. Indeed, engagement in care is measured and operationalised variously throughout the literature [44], with implications for results [45]. Self-report is the most commonly used measure of ART adherence but suffers from social desirability and recall biases [46]; viral

load is thus viewed as a more objective marker of adherence. Taken together, this thesis focusses on viral load given methodological considerations and as a robust clinical outcome and the ultimate goal of ART use. In addition, this thesis focusses on a single mental health outcome, depression, as a particularly common mental disorder [47] with well-established detrimental effects on ART adherence [20, 24].

1.3 Aim and objectives

The aim of this thesis is to provide insights into the patterns, predictors and impact of HIV-status disclosure among pregnant and postpartum women in the context of lifelong ART in South Africa, including considerations of stigma, social support, depression and unintended pregnancy.

Specific objectives are:

1. To describe patterns and predictors of HIV-status disclosure over time.
2. To examine the interplay between HIV-related stigma and perceived social support, and their impact on depressive symptoms.
3. To examine the impact of HIV-status disclosure on depressive symptoms, and the role of unintended pregnancy in this association.
4. To examine the impact of unintended pregnancy on HIV viral suppression, and the role of HIV-status disclosure in this association.
5. To examine the impact of HIV-status disclosure on HIV viral suppression.

This thesis focusses on three major outcomes: disclosure itself is examined as an outcome for Objective 1; depressive symptoms are investigated for Objectives 2 and 3; and viral load is the outcome of interest for Objectives 4 and 5. Throughout, this thesis aims to address the

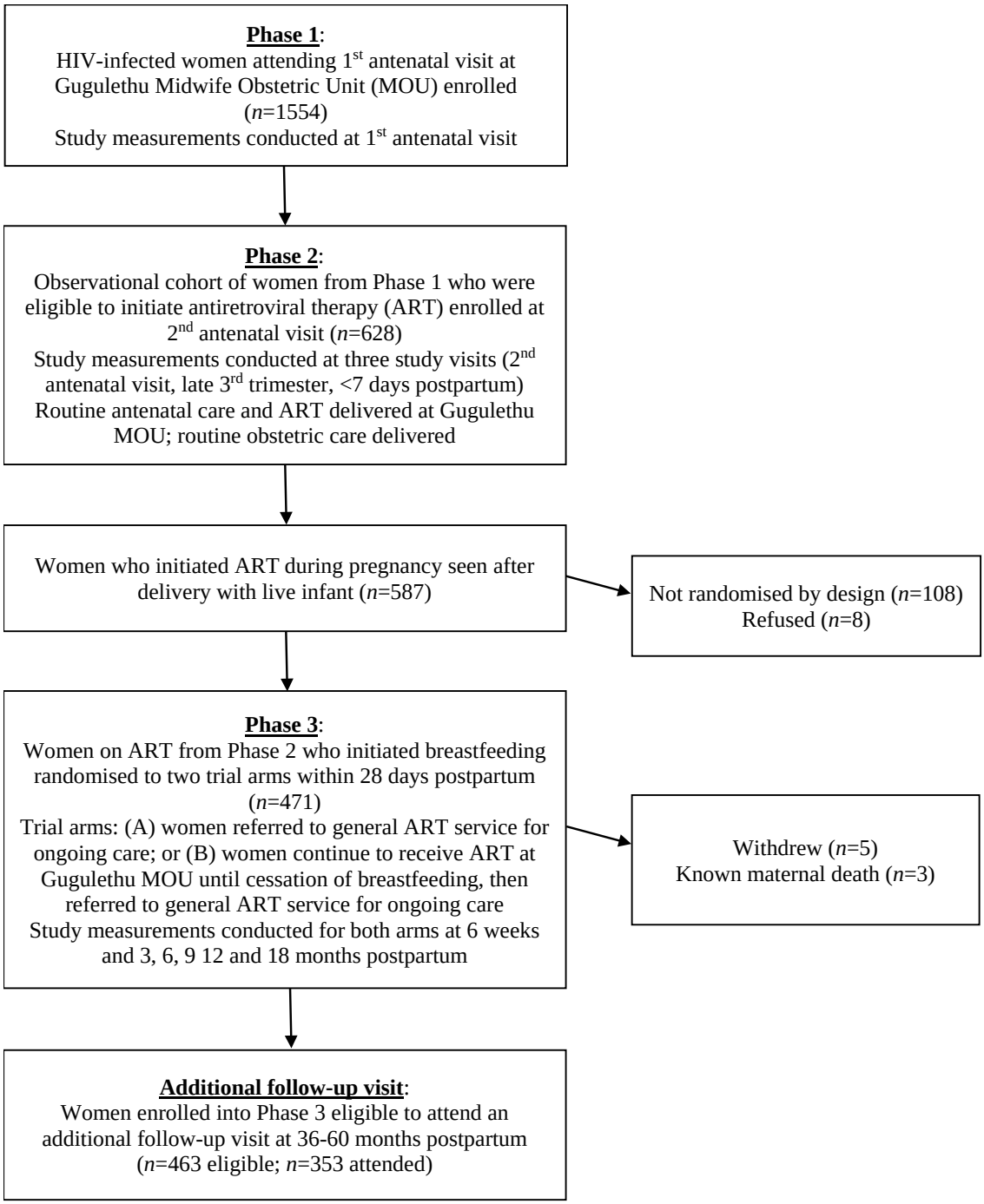
limitations which are alluded to above and are discussed further in Chapter 2, while positioning these findings within the context of lifelong ART in South Africa.

1.4 Data source

1.4.1 Maternal and Child Health – Antiretroviral Therapy (MCH-ART) study

Data for this thesis came from the Maternal and Child Health – Antiretroviral Therapy (MCH-ART) study [48, 49]. The MCH-ART study was a multi-phase implementation science study which sought to evaluate strategies for delivering HIV care and treatment services during the postpartum period. The study was conducted at a large primary care antenatal clinic in the former township of Gugulethu in Cape Town, South Africa. Participants were enrolled between March 2013 and June 2014, with follow-up visits conducted through May 2016. The study was conducted across three phases: Phase 1 was a cross-sectional evaluation of all HIV-infected women who were attending their first antenatal visit at the Midwife Obstetric Unit (MOU) at the Gugulethu Community Health Centre; Phase 2 was a longitudinal observational cohort study of Phase 1 women who were eligible to initiate ART, with participants attending up to three study visits during this phase; and Phase 3 was a randomised controlled trial of women from Phase 2 who opted to breastfeed postpartum. For the randomised controlled trial, women were randomised to either (A) attend general ART services for ongoing care, or (B) continue receiving ART at the MOU for the duration of breastfeeding, with women in both trial arms attending up to six study visits during postpartum follow-up. Follow-up for the study was later extended to include one additional study visit. Figure 1.2 presents a schema of these phases as well as the sample size enrolled into each phase. Different sub-samples are included in different analyses of this thesis, as described in each chapter.

Figure 1.2. Schema of the Maternal and Child Health – Antiretroviral Therapy (MCH-ART) study



For Phase 1, consecutive HIV-infected women who were entering antenatal care were approached and were eligible to participate if they were aged ≥18 years, were confirmed HIV-positive and pregnant, and were either established on ART or had not yet initiated ART or antiretroviral prophylaxis during the current pregnancy. For Phase 2, a subset of Phase 1

participants who were ART-eligible according to local guidelines were enrolled into antenatal follow-up. At the time of the study, ART eligibility was determined based on CD4 cell count or clinical disease staging until June 2013, after which all women entering antenatal care were eligible to initiate ART under Option B+ guidelines, with the majority of participants enrolled under Option B+ guidelines. The potential implications of context and changes in treatment guidelines are discussed in Chapter 2. For Phase 3 of the MCH-ART study, a subset of Phase 2 participants who had initiated ART and were breastfeeding at the first postpartum study visit were eligible for further postpartum follow-up. Eligible participants were randomly allocated at this study visit. Data from Phases 1-3 are included in Chapters 3-5 and in Chapter 7.

Follow-up for the study was later extended to 36-60 months postpartum. All women who had been enrolled into Phase 3 and who were not known to have died or to have withdrawn from the study were eligible for further follow-up. A total of 353 women were successfully contacted and attended one additional study visit between 36-60 months postpartum. Data from Phases 1-3 and from this additional study visit are included in Chapter 6.

The MCH-ART study was approved by the University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee and by Columbia University Medical Center's Institutional Review Board in New York. The secondary data analyses undertaken for this thesis were approved by the University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee. All women provided written informed consent prior to enrolment.

1.4.2 Overview of data included

Study measures collected as part of the MCH-ART study and the additional follow-up visit between 36-60 months postpartum are included in Appendix 1 and 2, respectively. Measures related to the primary focus of this thesis, HIV-status disclosure, were collected at all study measurement visits. Other major constructs of interest include unintended pregnancy (assessed at enrolment into the study) and HIV-related stigma and social support (data included from the 2nd antenatal study visit); demographic characteristics included were assessed at enrolment into the study. As stated above, the major outcomes of interest in this thesis are disclosure (Chapter 3), depressive symptoms (Chapters 4 and 5) and HIV viral load (Chapters 6 and 7). Depressive symptoms were measured at the 2nd antenatal study visit and at 6 weeks, 12 months, 18 months and 36-60 months postpartum. HIV viral load was measured at all study measurement visits. Additional information regarding the measures included is detailed in the results chapters (Chapters 3-7).

An issue which may be related to each of these constructs is that of intimate partner violence. Violence within intimate partnerships is prevalent in South Africa [50], and a major reason for non-disclosure to sexual partners is the fear of violence [51, 52]. In addition, violence has been observed to be associated with stigma [53] and is a well-documented predictor of depression [54-56]. Although an in-depth exploration of intimate partner violence is beyond the scope of this thesis, it should be noted throughout that these data arose from a setting in which violence is common and may have far-reaching effects on women's health and well-being.

1.4.3 Overview of analytic methods

The body of work contained in this thesis aims to provide an in-depth exploration of HIV-status disclosure and related constructs. However, differences in the measures included in analyses and analytic methods used arose over time as this work progressed. An example is the measure of unintended pregnancy used: in some analyses, a single question was used to assess pregnancy intentions and in others a more sophisticated measure was used. These two measures have been compared within this cohort with high levels of concordance [41], thus the conclusions are likely robust despite the different measures used. For all analyses, potential confounders were defined *a priori,* and typically included measures of socioeconomic status, age and relationship status. When examining viral load outcomes, previous viral load results and duration on ART were controlled for as critical determinants of viral suppression. For postpartum viral load outcomes, allocation in the MCH-ART trial was included in multivariable models in order to control for design effect.

1.5 Overview and structure of this thesis

This introductory chapter introduces the topic of HIV-status disclosure. It includes a brief overview of the issues that this thesis will address and the rationale and aim and objectives. As this work includes only secondary analysis of data, this chapter includes a description of the broader study from which these data arise, and a brief overview of the measures included and analytic methods used. Following the introductory chapter, this thesis includes a literature review, five results chapters and a discussion chapter summarising the contributions of this work as well as recommendations for research and practice.

Chapter 2 provides the background to this thesis in a review of the literature on each of the major constructs of interest which form the basis of this thesis: disclosure, stigma, social

support, mental health and unintended pregnancy. Details regarding the methodology and focus of this review are provided at the beginning of the chapter. Five results chapters, in the form of published papers or papers that have been submitted for publication, are presented in Chapters 3-7. These map to the objectives of this thesis. A summary of these results chapters, including the primary focus and methodologies used, is presented in Table 1.2, below.

Table 1.2 Summary of thesis results chapters, including outcome variables and methodologies

Chapter	Objective	Publication title	Outcome	Methodology
3	1	Patterns and predictors of HIV-status disclosure among pregnant women in South Africa: dimensions of disclosure and influence of social and economic circumstances	Disclosure	Cross-sectional analysis at one timepoint during pregnancy, and time-to-event analyses during pregnancy and postpartum
4	2	Social support, stigma and antenatal depression among HIV-infected pregnant women in South Africa	Depressive symptoms	Cross-sectional analysis at one timepoint during pregnancy
5	3	HIV-status disclosure and depression in the context of unintended pregnancy among South African women	Depressive symptoms	Analyses at three timepoints during pregnancy and postpartum, using cumulative reports of disclosure up to each timepoint
6	4	Long-term effects of unintended pregnancy on antiretroviral therapy outcomes among South African women living with HIV	HIV viral load	Repeated measures analysis of HIV viral load results from 6 weeks through 36-60 months postpartum
7	5	Impact of HIV-status disclosure on viral load during pregnancy and postpartum in Cape Town, South Africa	HIV viral load	Analyses at three timepoints during pregnancy and postpartum, using cumulative reports of disclosure up to each timepoint

Chapter 3 addresses the first objective of this thesis by describing patterns and predictors of disclosure during pregnancy and postpartum. This chapter includes a strong methodological focus in order to address limitations of research to date. First, these analyses use both cross-

sectional and longitudinal data to examine patterns of disclosure, in contrast to the majority of research to date which has relied primarily on cross-sectional data. In addition, the chapter uses a novel analytic technique to examine patterns of disclosure in order to address a further limitation of research to date: the widespread focus on disclosure to any versus no persons, or the focus on disclosure to a sexual partner only. This chapter describes how disclosure forms two separate dimensions in this sample of women, specifically disclosure to a male partner, and disclosure to family/community members. Based on these findings, disclosure was analysed using these separate dimensions in subsequent chapters, thereby setting the scene for testing the assumption that the benefits of disclosure are consistent across the person(s) to whom individuals disclose.

Chapter 3 additionally highlights that social and economic circumstances are central determinants of disclosure. Given this finding, factors such as relationship status and unintended pregnancy were explored as key determinants and potential effect modifiers of the major constructs of interest in this thesis in subsequent chapters. This chapter thus provides the basis for testing the assumption that the benefits of disclosure are universally beneficial rather than potentially differing across different sub-groups. The chapter concludes by arguing that further high-quality evidence of the impact of disclosure on HIV and health-related outcomes is needed in order to inform counselling messaging and intervention efforts; the impact of disclosure on depression and viral load were thus explored in subsequent chapters. These subsequent chapters include investigations of the assumptions that (i) disclosure is universally beneficial with (ii) effects that are consistent over time, and (iii) that these benefits are consistent across the person(s) to whom individuals disclose.

Chapter 4 addresses the second objective of this thesis by exploring how social support and stigma are interrelated, and how they affect depression during pregnancy. As argued above, both social support and stigma are central to discussions of disclosure; indeed, non-disclosure has been described as a manifestation of stigma [57]. The impacts of social support and stigma on depression have been explored separately, but there are few considerations of how these constructs may be interrelated. This chapter thus describes the interrelationships among these factors, but also highlights stigma as an effect modifier in the association between social support and depressive symptoms, speaking to the profound impact of stigma in this context, and again speaking to the importance of considering sub-groups in exploring the effects of these factors.

Chapter 5 addresses the third objective of this thesis by exploring the impact of disclosure on depressive symptoms during pregnancy and postpartum, as well as the role of pregnancy intention in this relationship. These analyses were restricted to women who had been newly-diagnosed HIV-positive during the pregnancy. As described above, a new HIV diagnosis during pregnancy may heighten women's vulnerability and may be further compounded by an unintended pregnancy, but there is limited quantitative evidence for the effects of unintended pregnancy on maternal health and well-being. Disclosure has been described as an important factor in the evolution of coming to terms with a new HIV diagnosis [58], thus the impact of disclosure was explored in this group of newly-diagnosed women. Chapter 5 empirically tests each of the assumptions described above: (i) that disclosure is universally beneficial, by exploring unintended pregnancy as a potential modifier of the association between disclosure and depression; (ii) that the effects of disclosure are consistent over time, by assessing these associations at three different timepoints; and (iii) that the benefits of disclosure are consistent across the person(s) to whom individuals disclose, by exploring the

effects of disclosure to a male partner and to family/community members separately, based on the findings presented in Chapter 3. Chapter 5 describes how unintended pregnancy modifies the impact of disclosure to a male partner on depressive symptoms during pregnancy, providing strong evidence for the profound impact of an unintended pregnancy on women's mental health.

Chapter 6 addresses the fourth objective of this thesis. Given the impact of unintended pregnancy on mental health outcomes presented in Chapter 5, this chapter explores the long-term effects of an unintended pregnancy on HIV treatment outcomes. Specifically, the chapter explores the impact of unintended pregnancy on viral load during the postpartum period to provide quantitative evidence for the profound effects of an unintended pregnancy on women's health. This chapter also examines the role of disclosure to a male partner in this association, given the effect modification described in Chapter 5. This chapter provides strong and novel evidence for the long-term impact of an unintended pregnancy on HIV treatment outcomes in this population, speaking not only to the importance of preventing unintended pregnancies to prevent MTCT, but also to promote women's health in the postpartum period.

Chapter 7 addresses the fifth and final objective of this thesis by exploring the impact of disclosure on viral load. This chapter tests the three assumptions that this thesis aims to critique: (i) that disclosure is universally beneficial, by exploring the effect of disclosure in different sub-groups; (ii) that the effects of disclosure are consistent over time, by investigating these effects at three different timepoints; and (iii) that the benefits of disclosure are consistent across the person(s) to whom individuals disclose, by exploring each of disclosure to a male partner and disclosure to family/community members, again based on the

results presented in Chapter 3. Given the heightened vulnerability that results from a new HIV diagnosis during pregnancy, one of the sub-groups that was explored in testing the first assumption was the timing of HIV diagnosis (before versus during pregnancy), with important differences in results. Overall, this chapter provides strong evidence against the three assumptions presented above by describing a complex association between disclosure and viral load that is modified by three factors: (i) timing of HIV diagnosis (before versus during pregnancy); (ii) relationship to the person(s) to whom women disclose, and (iii) in the case of disclosure to a male partner, relationship status. Consistent with Chapters 3 and 5, these results speak to the critical role of women's circumstances in considerations of these constructs.

Finally, Chapter 8 summarises the empirical findings of this thesis and considers the public health implications of these results. This chapter concludes with recommendations for both research and practice, based on the evidence presented in this thesis against the three assumptions described above.

1.6 Public health significance

HIV-status disclosure has long been acknowledged as an important factor in HIV care, with potential benefits for both population and individual health. However, there are important limitations in research to date and current policy and practice. This thesis aims to critique three widely-held assumptions regarding the benefits of disclosure and to provide quantitative insights into other factors that are interrelated with disclosure and are similarly important in HIV care. Given the recent roll-out of Option B+ guidelines in South Africa and other settings, this research is timely. Public health approaches are centred on population-level interventions and are typically not tailored to the individual. However, this thesis will argue

that disclosure is ultimately an individual issue that occurs within social relationships, and that counselling messaging needs to be tailored to the individual. Second, stigma is widely acknowledged as a pervasive and harmful factor [47, 57]; this thesis will provide further quantitative evidence for this viewpoint. Finally, this thesis will highlight pregnancy as a critical window, both as a period during which disclosure may affect viral load and, if the pregnancy is unintended, as a profound determinant of adverse outcomes in the long term. Taken together, this thesis will argue that although much of the progress in preventing MTCT in South Africa and globally has been due to population-wide public health approaches, the individual cannot be ignored in our response to the HIV pandemic [59] and must be central in research, policy and practice.

References

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS Data 2018. Geneva: UNAIDS; 2018.
2. South African National Department of Health. The 2015 National Antenatal Sentinel HIV & Syphilis Survey Report. Pretoria: South African National Department of Health; 2017.
3. Hawkins D, Blott M, Clayden P, de Ruiter A, Foster G, Gilling-Smith C, et al. Guidelines for the management of HIV infection in pregnant women and the prevention of mother-to-child transmission of HIV. HIV Med. 2005;6(Suppl 2):107-148.
4. Joint United Nations Programme on HIV/AIDS (UNAIDS). 2015 Progress Report on the Global Plan towards the elimination of new HIV infections among children and keeping their mothers alive. Geneva: UNAIDS; 2015.
5. Burton R, Giddy J, Stinson K. Prevention of mother-to-child transmission in South Africa: an ever-changing landscape. Obstet Med. 2015;8(1):5-12.
6. Western Cape Department of Health. The Western Cape consolidated guidelines for HIV treatment: prevention of mother-to-child transmission of HIV (PMTCT), children, adolescents and adults. Cape Town: Western Cape Department of Health; 2018.
7. World Health Organization. PMTCT strategic vision 2010-2015: preventing mother-to-child transmission of HIV to reach the UNGASS and Millennium Development Goals. Geneva: World Health Organization; 2010.
8. Simoni JM, Kurth AE, Pearson CR, Pantalone DW, Merrill JO, Frick PA. Self-report measures of antiretroviral therapy adherence: a review with recommendations for HIV research and clinical management. AIDS Behav. 2006;10:227-245.
9. Bärnighausen T, Chaiyachati K, Chimbindi N, Peoples A, Haberer J, Newell M-L. Interventions to increase antiretroviral adherence in sub-Saharan Africa: a systematic review of evaluation studies. Lancet Infect Dis. 2011;11:942-951.
10. Mandelbrot L, Tubiana R, Le Chenadec J, Dollfus C, Faye A, Pannier E, et al. No perinatal HIV-1 transmission from women with effective antiretroviral therapy starting before conception. Clin Infect Dis. 2015;61(11):1715-1725.
11. Goga A, Sherman G, Chirinda W, Ng'oma K, Bhardwaj S, Doherty T, et al. Eliminating mother-to-child transmission of HIV in South Africa, 2002-2016: progress, challenges and the Last Mile Plan. South African Health Review. 2017;2017(1):137-146.
12. Goga AE, Dinh T-H, Jackson DJ, Lombard C, Delaney KP, Puren A, et al. First population-level effectiveness evaluation of a national programme to prevent HIV transmission from mother to child, South Africa. J Epidemiol Community Health. 2015;69:240-248.
13. Mahy M, Penazzato M, Ciaranello A, Mofenson L, Yiannoutsos C, Davies M-A, et al. Improving estimates of children living with HIV from the Spectrum AIDS Impact Model. AIDS. 2017;31(Suppl 1):S13-S22.
14. Ahmed S, Kim MH, Abrams EJ. Risks and benefits of lifelong antiretroviral treatment for pregnant and breastfeeding women: a review of the evidence for the Option B+ approach. Curr Opin HIV AIDS. 2013;8:474-489.

15. Nachega JB, Uthman OA, Anderson J, Peltzer K, Wampold S, Cotton MF, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. AIDS. 2012;26:2039-2052.
16. Ngarina M, Popenoe R, Kilewo C, Biberfeld G, Ekstrom AM. Reasons for poor adherence to antiretroviral therapy postnatally in HIV-1 infected women treated for their own health: experiences from the Mitra Plus study in Tanzania. BMC Public Health. 2013;13:450.
17. Luzuriaga K, Mofenson LM. Challenges in the elimination of pediatric HIV-1 infection. N Engl J Med. 2016;374:761-770.
18. Phillips T, McNairy ML, Zerbe A, Myer L, Abrams EJ. Postpartum transfer of care among HIV-infected women initiating antiretroviral therapy during pregnancy. J Acquir Immune Defic Syndr. 2015;70(3):e102-e109.
19. Knettel BA, Cichowitz C, Samwel Ngocho J, Knippler ET, Chumba LN, Mmbaga BT, et al. Retention in HIV care during pregnancy and the postpartum period in the Option B+ era: systematic review and meta-analysis of studies in Africa. J Acquir Immune Defic Syndr. 2018;77:427-438.
20. Heestermans T, Browne JL, Aitken SC, Vervoort SC, Klipstein-Grobusch K. Determinants of adherence to antiretroviral therapy among HIV-positive adults in sub-Saharan Africa: a systematic review. BMJ Glob Health. 2016;1:e000125.
21. Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J, et al. A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women. PLoS ONE. 2014;9(11):e111421.
22. Govindasamy D, Ford N, Kranzer K. Risk factors, barriers and facilitators for linkage to antiretroviral therapy care: a systematic review. AIDS. 2012;26:2059-2067.
23. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. J Int AIDS Soc. 2013;16:18588.
24. O'Hiarlaithe M, Grede N, de Pee S, Bloem M. Economic and social factors are some of the most common barriers preventing women from accessing maternal and newborn child health (MNCH) and prevention of mother-to-child transmission (PMTCT) services: a literature review. AIDS Behav. 2014;18:S516-S530.
25. Obermeyer CM, Baijal P, Pegurri E. Facilitating HIV disclosure across diverse settings: a review. Am J Public Health. 2011;101(6):1011-1023.
26. Norman A, Chopra M, Kadiyala S. Factors related to HIV disclosure in 2 South African communities. Am J Public Health. 2007;97:1775-1781.
27. Chaudoir SR, Fisher JD. The Disclosure Processes Model: understanding disclosure decision making and postdisclosure outcomes among people living with a concealable stigmatized identity. Psychol Bull. 2010;136(2):236-256.
28. Chaudoir SR, Fisher JD, Simoni JM. Understanding HIV disclosure: a review and application of the Disclosure Processes Model. Soc Sci Med. 2011;72(10):1618-1629.
29. Bott S, Obermeyer CM. The social and gender context of HIV disclosure in sub-Saharan Africa: a review of policies and practices. SAHARA J. 2013;10(Suppl 1):S5-S16.

30. Vyavaharkar M, Moneyham L, Corwin S, Tavakoli A, Saunders R, Annang L. HIV-disclosure, social support, and depression among HIV-infected African American women living in the rural southeastern United States. AIDS Educ Prev. 2011;23(1):78-90.
31. Omonaiye O, Kusljic S, Nicholson P, Manias E. Medication adherence in pregnant women with human immunodeficiency virus receiving antiretroviral therapy in sub-Saharan Africa: a systematic review. BMC Public Health. 2018;18:805.
32. Hardon A, Vernooij E, Bongololo-Mbera G, Cherutich P, Desclaux A, Kyaddondo D, et al. Women's views on consent, counseling and confidentiality in PMTCT: a mixed-methods study in four African countries. BMC Public Health. 2012;12:26.
33. Dima AL, Stutterheim SE, Lyimo R, de Bruin M. Advancing methodology in the study of HIV status disclosure: the importance of considering disclosure target and intent. Soc Sci Med. 2014;108:166-174.
34. Smith R, Rossetto K, Peterson BL. A meta-analysis of disclosure of one's HIV-positive status, stigma and social support. AIDS Care. 2008;20(10):1266-1275.
35. Kasenga F, Hurtig A-K, Emmelin M. HIV-positive women's experiences of a PMTCT programme in rural Malawi. Midwifery. 2010;26:27-37.
36. Miller ES, Yee LM, Dorman RM, McGregor DV, Sutton SH, Garcia PM, et al. Is maternal disclosure of HIV serostatus associated with a reduced risk of postpartum depression? Am J Obstet Gynecol. 2016;215:521.e1-5.
37. Tsui AO, McDonald-Mosley R, Burke AE. Family planning and the burden of unintended pregnancies. Epidemiol Rev. 2010;32:152-174.
38. Crankshaw TL, Voce A, King RL, Giddy J, Sheon NM, Butler LM. Double disclosure bind: complexities of communicating an HIV diagnosis in the context of unintended pregnancy in Durban, South Africa. AIDS Behav. 2014;18:S53-S59.
39. Lewinsohn R, Crankshaw T, Tomlinson M, Gibbs A, Butler L, Smit J. "This baby came up and then he said, "I give up!": The interplay between unintended pregnancy, sexual partnership dynamics and social support and the impact on women's well-being in KwaZulu-Natal, South Africa. Midwifery. 2018;62:29-35.
40. Adeniyi OV, Ajayi AI, Moyaki MG, Goon DT, Avramovic G, Lambert J. High rate of unplanned pregnancy in the context of integrated family planning and HIV care services in South Africa. BMC Health Serv Res. 2018;18(1):140.
41. Iyun V, Brittain K, Phillips TK, le Roux S, Mcintyre JA, Zerbe A, et al. Prevalence and determinants of unplanned pregnancy in HIV-positive and HIV-negative pregnant women in Cape Town, South Africa: a cross-sectional study. BMJ Open. 2018;8:e019979.
42. Myer L, Phillips TK, Hsiao N-Y, Zerbe A, Petro G, Bekker L-G, et al. Plasma viraemia in HIV-positive pregnant women entering antenatal care in South Africa. J Int AIDS Soc. 2015;18:20045.
43. South African National Department of Health. National contraception and fertility planning policy and service delivery guidelines. Pretoria: South African National Department of Health; 2012.
44. Rollins NC, Becquet R, Orne-Gliemann J, Phiri S, Hayashi C, Baller A, et al. Defining and analyzing retention-in-care among pregnant and breastfeeding HIV-infected women: unpacking the data to interpret and improve PMTCT outcomes. J Acquir Immune Defic Syndr. 2014;67(Suppl 2):S150-S156.

45. Grimsrud AT, Cornell M, Egger M, Boulle A, Myer L. Impact of definitions of loss to follow-up (LTFU) in antiretroviral therapy program evaluation: variation in the definition can have an appreciable impact on estimated proportions of LTFU. J Clin Epidemiol. 2013;66(9):1006-1013.
46. Berg KM, Arnsten JH. Practical and conceptual challenges in measuring antiretroviral adherence. J Acquir Immune Defic Syndr. 2006;43(Suppl 1):S79-S87.
47. Nachega JB, Morroni C, Zuniga JM, Sherer R, Beyrer C, Solomon S, et al. HIV-related stigma, isolation, discrimination, and serostatus disclosure: a global survey of 2035 HIV-infected adults. J Int Assoc Physicians AIDS Care. 2012;11(3):172-178.
48. Myer L, Phillips TK, Zerbe A, Ronan A, Hsiao N-Y, Mellins CA, et al. Optimizing antiretroviral therapy (ART) for maternal and child health (MCH): rationale and design of the MCH-ART study. J Acquir Immune Defic Syndr. 2016;72:S189-S196.
49. Myer L, Phillips TK, Zerbe A, Brittain K, Lesosky M, Hsiao N-Y, et al. Integration of postpartum healthcare services for HIV-infected women and their infants in South Africa: a randomised controlled trial. PLoS Med. 2018;15(3):e1002547.
50. Bernstein M, Phillips T, Zerbe A, McIntyre JA, Brittain K, Petro G, et al. Intimate partner violence experienced by HIV-infected pregnant women in South Africa: a cross-sectional study. BMJ Open. 2016;6:e011999.
51. Karamagi CAS, Tumwine JK, Tylleskar T, Heggenhougen K. Intimate partner violence against women in eastern Uganda: implications for HIV prevention. BMC Public Health. 2006;6:284.
52. Maeri I, El Ayadi A, Getahun M, Charlebois E, Akatukwasa C, Tumwebaze D, et al. "How can I tell?" Consequences of HIV status disclosure among couples in eastern African communities in the context of an ongoing HIV "test-and-treat" trial. AIDS Care. 2016;28(Suppl 3):59-66.
53. Fiorentino M, Sagaon-Teyssier L, Ndiaye K, Suzan-Monti M, Mengue M-T, Vidal L, et al. Intimate partner violence against HIV-positive Cameroonian women: prevalence, associated factors and relationship with antiretroviral therapy discontinuity – results from the ANRS-12288 EVOLCam survey. Womens Health. 2019;15:1745506519848546.
54. Nyamukoho E, Mangezi W, Marimbe B, Verhey R, Chibanda D. Depression among HIV positive pregnant women in Zimbabwe: a primary health care based cross-sectional study. BMC Pregnancy Childbirth. 2019;19:53.
55. Peltzer K, Rodriguez VJ, Lee TK, Jones D. Prevalence of prenatal and postpartum depression and associated factors among HIV-infected women in public primary care in rural South Africa: a longitudinal study. AIDS Care. 2018;30(11):1372-1379.
56. Tsai AC, Tomlinson M, Comulada WS, Rotheram-Borus MJ. Intimate partner violence and depression symptom severity among South African women during pregnancy and postpartum: population-based prospective cohort study. PLoS Med. 2016;13(1):e1001943.
57. Turan B, Hatcher AM, Weiser SD, Johnson MO, Rice WS, Turan JM. Framing mechanisms linking HIV-related stigma, adherence to treatment, and health outcomes. Am J Public Health. 2017;107(6):863-869.
58. Medley AM, Kennedy CE, Lunyolo S, Sweat MD. Disclosure outcomes, coping strategies, and life changes among women living with HIV in Uganda. Qual Health Res. 2009;19(12):1744-1754.

59. Remien RH, Mellins CA. Long-term psychosocial challenges for people living with HIV: let's not forget the individual in our global response to the pandemic. AIDS. 2007;21(Suppl 5):S55-S63.

Chapter 2: Literature review

Overview

The purpose of this literature review is to establish the conceptual background for this thesis by providing an orientation to and summary of existing knowledge related to HIV-status disclosure. In this thesis, disclosure is presented as both an exposure of interest and an outcome. This review summarises relevant knowledge related to four additional constructs of interest: stigma, social support, depression and unintended pregnancy. Stigma and social support are closely related to disclosure; indeed, each may be both a predictor and an outcome of disclosure. Mental health is a similarly related psychosocial factor that may be improved by disclosure, and depression is the second outcome of interest in this thesis. Finally, an important but understudied issue in the field of disclosure among pregnant women is that of unintended pregnancy. Each of these factors are discussed in this review as critical constructs related to disclosure and as important factors in prevention of mother-to-child transmission (PMTCT) care, and the review includes an overview of impacts on the third and final outcome of interest: HIV viral suppression. The review is structured according to the objectives of this thesis and addresses themes that are relevant to the results chapters which follow. Where appropriate, tables are used to summarise the results of selected primary quantitative studies to give an overview of findings.

Section 2.1 presents a brief overview of the conceptual underpinnings of this thesis, including the theoretical understanding of disclosure on which this work is based as well as conceptual frameworks related to determinants of antiretroviral therapy (ART) adherence and to types of stigma. The purpose of this section is not to provide an exhaustive review of all theoretical

frameworks through which these constructs can be viewed but rather to briefly describe the conceptual frameworks on which this thesis draws to orientate readers to this thinking. Sections 2.2 to 2.4 review literature to provide context for the objectives of this thesis. Section 2.2 focusses on patterns and predictors of disclosure, providing background for Chapter 3. This section provides a summary of selected literature but also highlights the methodological limitations in the existing literature, providing a strong basis for the methodological approach taken in this thesis. To provide background for Chapters 4-6, stigma, social support, mental health and unintended pregnancy are reviewed in Section 2.3. As alluded to above and argued further in this section, stigma and social support may be both determinants and outcomes of disclosure and are themselves important determinants of HIV-related outcomes. The literature on mental health provides background for Chapters 4 and 5 and points to links with each of stigma, social support and disclosure while similarly highlighting the importance of mental health in HIV care. Literature on unintended pregnancy is summarised to provide additional background for Chapters 5 and 6.

Section 2.4 reviews the potential impacts of disclosure along the HIV care cascade. Although not the focus of this thesis, this section provides a summary of literature pointing to associations between disclosure and outcomes such as entry into and engagement in HIV care before summarising and critiquing existing knowledge on associations with adherence and viral load. As argued in Chapter 1, viral load is arguably a more objective marker of adherence, and viral suppression is the ultimate goal of ART use for both prevention and treatment. This thesis focusses on viral load only but literature on adherence is summarised for two purposes: (i) as an important behavioural intermediate between disclosure and viral suppression; and (ii) as a means of contrasting this literature to findings regarding viral load.

Finally, Section 2.5 highlights limitations of the current evidence, points to the research needs that the subsequent results chapters aim to address and provides some context to this work. The data on which this thesis is based arise from a particular point in the HIV epidemic in South Africa, and it is critical to recognise the impact that this, along with changing treatment guidelines, has on the constructs on which this thesis focusses. More weight is given to relatively recent studies throughout this literature review, given these changes over time, but this section speaks to how context may have impacted on these constructs over time, and what impacts additional changes may have going forward.

Methodology

This review is not intended to be systematic or exhaustive but rather provides an overview of key points and gaps in our understanding of disclosure and critically interrelated constructs. The primary focus is on literature in the context of PMTCT, but the review also includes articles from general adult populations where these contribute important knowledge. Similarly, most literature reviewed is from low- and middle-income country (LMIC) settings, given that the data on which this thesis is based arise from South Africa, but literature from high-income countries is included where this contributes meaningfully. PubMed and PsycINFO were searched for relevant literature, and reference lists were checked for additional key publications.

Many early papers focussed on the ethics of disclosure. These papers were excluded as they are beyond the scope of this thesis. Recently, there has been much research on disclosing to perinatally HIV-infected children. As the focus of this thesis is on women disclosing their own HIV-status to others within their social network, these papers were excluded, as were articles which focussed on disclosure to medical professionals. HIV-infected women may be

less likely to disclose their HIV-status compared to HIV-uninfected women [1, 2]; this thesis focusses only on HIV-infected women. The two potential benefits of disclosure on which this thesis focusses are improved mental health and viral suppression. Importantly, HIV-status disclosure may confer other benefits, including behaviours such as consistent condom use [3] and appropriate infant feeding [4]. These behaviours are beyond the scope of this thesis and will not be discussed in this review.

2.1 Conceptual underpinnings

2.1.1 The disclosure process

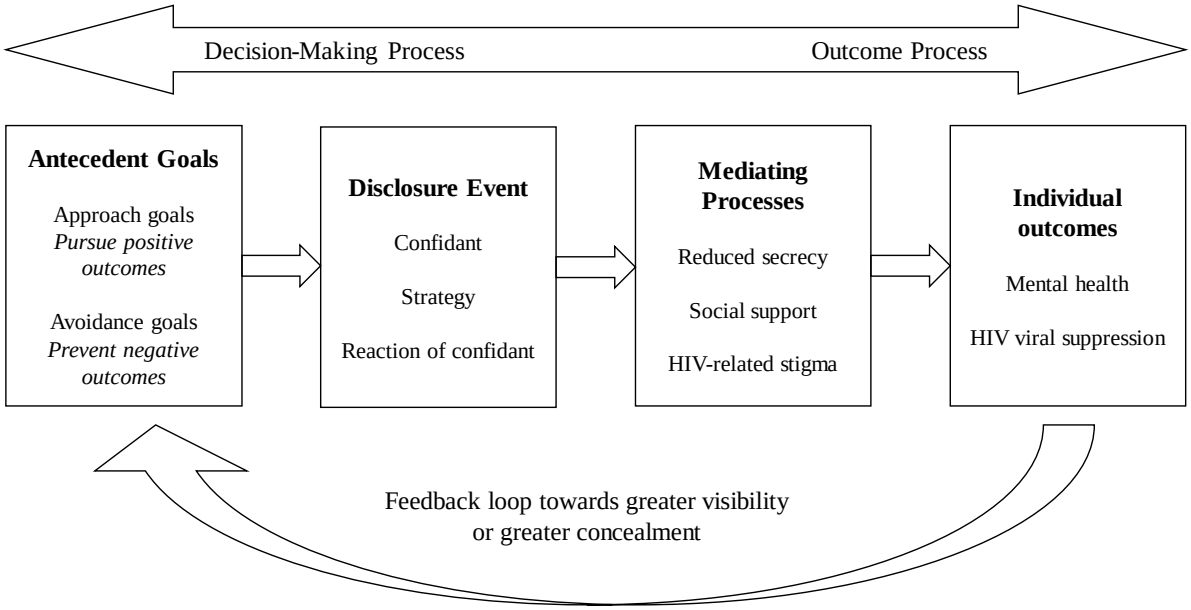
Following an HIV-positive diagnosis, individuals must decide whether, how and to whom to disclose their HIV status [5]. Disclosure is inherently a sequential process that occurs over time [6, 7]. Indeed, much of the literature operationalises disclosure as any versus no disclosure [8]. Despite this, it has been argued that the disclosure process is neither singular nor uniform: rather, disclosure acts to different individuals may not be interchangeable indicators of a single underlying process [8, 9]. Disclosure may be either voluntary or involuntary, but few studies have differentiated between these [8, 9]. As the data on which this thesis is based include only voluntary acts of disclosure, this thesis focusses only on voluntary disclosure.

The disclosure act has been described as fluid and dynamic [10]. Rather than being a discrete event, it may occur as a gradual process of slowly revealing an HIV-positive diagnosis to a particular individual over time. In addition, disclosure acts may occur in different ways [6]. Women in sub-Saharan Africa, for example, have described sometimes disclosing indirectly, for example by not hiding their antiretroviral drugs or by taking ART in front of others to whom they have not disclosed [11, 12]. A further strategy among women testing HIV-

positive during antenatal care is to subsequently attend couples counselling and testing with a male partner. With this strategy, women are able to 'discover' their HIV-positive status in the presence of their partner and with a counsellor who acts as an intermediary [11]. The disproportionately high burden of disclosure which women face and the barriers that are specific to disclosing to a male partner are discussed under Section 2.2.6, below.

The conceptual underpinning of this thesis is the Disclosure Processes Model [13, 14]. This model has been posited as a theoretical framework to understand when and why disclosure is beneficial. Given that this thesis aims to critique assumptions regarding disclosure as a universally and consistently beneficial act, a framework that focusses on when and why disclosure is beneficial is particularly relevant to this work. The model depicts the processes involved in one disclosure event that is situated within a lifelong series of disclosure events, and a feedback loop is included to depict the fact that one disclosure event can affect subsequent disclosure trajectories. Specifically, individuals who experience positive outcomes following disclosure may become more open about their HIV status, while negative outcomes may lead to greater concealment. Although neither aspects of the disclosure event itself nor responses to disclosure are addressed in this thesis, the framework is included as a useful overarching understanding of the disclosure process. Figure 2.1 presents the Disclosure Processes Model, adapted for this thesis.

Figure 2.1 Disclosure Processes Model, adapted for this thesis [13, 14]

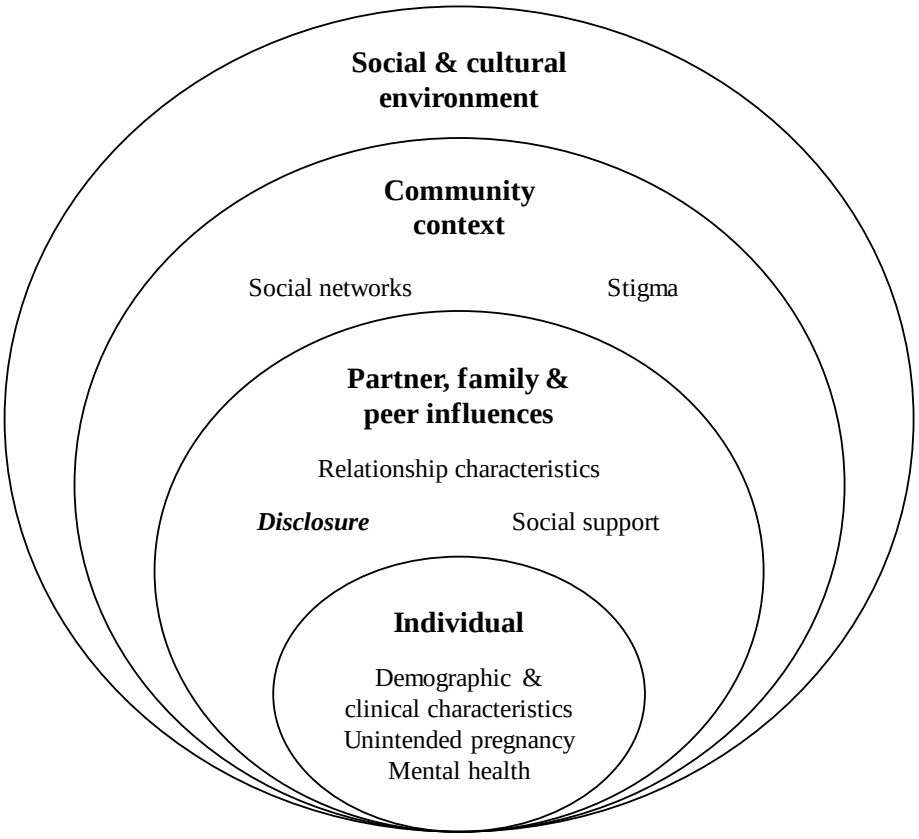


The decision-making process begins with antecedent goals: individuals may disclose to pursue positive outcomes (approach goals, for example social support) or to prevent negative outcomes (avoidance goals, for example HIV-related stigma). After the decision to disclose is the disclosure event itself. Although not assessed in the study from which these data arise, the reaction of the person(s) to whom individuals disclose ('confidants' in the figure above) may be a critical determinant of whether the disclosure event leads to beneficial outcomes. Along with being antecedent goals, social support and stigma may be mediators of the associations between disclosure and individual outcomes. Specifically, disclosure may lead to increased social support, or to social rejection. A further mediating process is that of reduced secrecy around HIV care engagement and ART use. Limited disclosure may lead to poor treatment outcomes through secrecy, and reduced secrecy following disclosure may therefore be a mediator of improved outcomes. The outcomes that are the focus of this thesis are at the individual level: depression and viral suppression. Importantly, there may be other individual-level benefits of disclosure, as well as population-level benefits, but these are beyond the scope of this thesis.

2.1.2 Determinants of ART adherence

Figure 2.2 presents a conceptual framework reflecting determinants of ART adherence in the context of PMTCT, adapted for this thesis. This socio-ecological framework reflects the fact that determinants of adherence are multifaceted and occur at multiple levels [15]. This framework is a specific manifestation of the broader ecological framework which is widely posited in public health. The framework is included here as an overarching understanding of factors that may affect adherence among HIV-infected pregnant and postpartum women, with disclosure included as one of these factors. As will be argued in this thesis, disclosure is a complex act that occurs within social relationships. An overarching framework of other determinants of adherence is thus useful to situate disclosure within these broader socio-ecological factors. Importantly, Figure 2.2 is not an exhaustive framework reflecting all determinants of adherence; instead, the framework is limited to factors included in this thesis.

Figure 2.2 Socio-ecological framework of determinants of antiretroviral therapy (ART) adherence, adapted for this thesis [15]

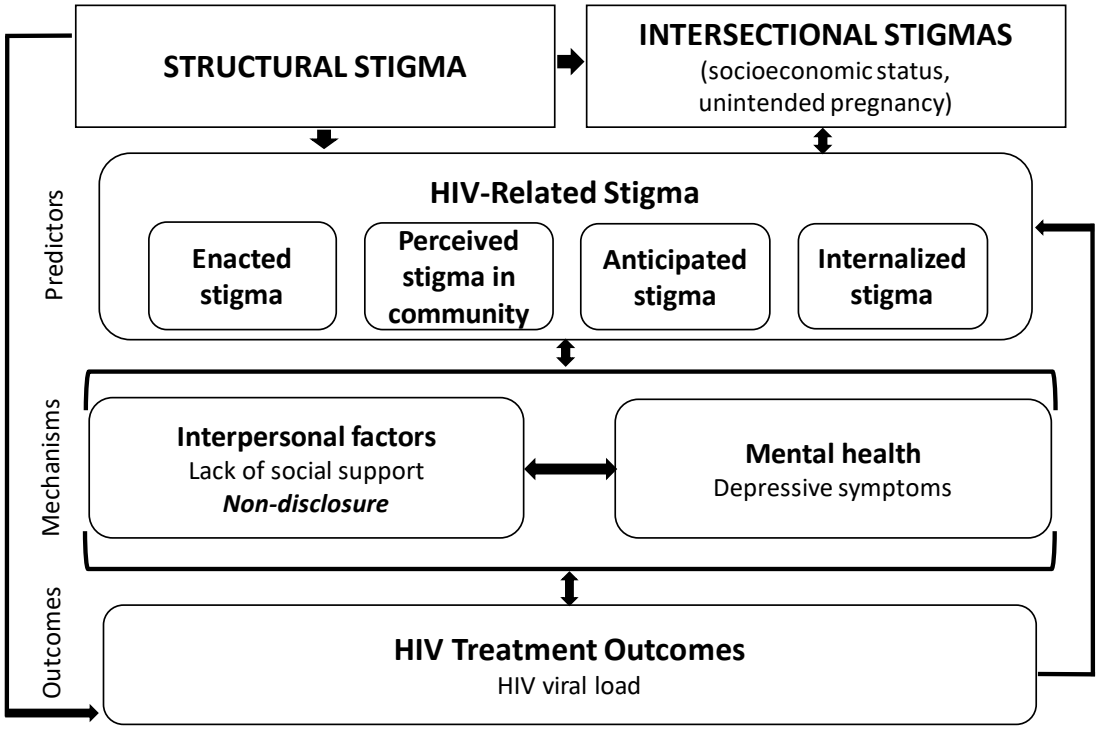


Qualitative work from South Africa has described the disclosure process as embedded in a particular context and occurring against a backdrop of changing intrapersonal and interpersonal circumstances [10]. This thesis includes factors at the community; partner, family and peer; and individual levels, but all were assessed at the level of the individual. Specifically, although factors such as stigma and support operate at the community and interpersonal levels, these factors were measured using women's reports of stigma and the availability of social support. Of note is that each of the factors in the above framework may be related to both disclosure and ART adherence. Further, all of these factors are situated within a broader social, cultural and political context which may affect the prevalence of disclosure [7], although these more distal factors were not assessed. The impact of these broader factors is discussed in Section 2.5, below.

2.1.3 Types of stigma

A final relevant framework is one describing different types of stigma [16]. Although the impact of stigma itself is beyond the scope of this thesis, non-disclosure is often treated as a proxy for stigma and is arguably a manifestation of stigma [16]. Indeed, the framework includes non-disclosure as a mediator between stigma and treatment outcomes. Many of the constructs that are central to this thesis are represented in this framework, including disclosure, different types of stigma, social support, mental health, unintended pregnancy and HIV treatment outcomes; as such, this framework is particularly relevant to this work. Figure 2.3 presents this framework, adapted for this thesis.

Figure 2.3 Framework of types of stigma and their impact on treatment outcomes, adapted for this thesis [16].



The types of stigma reflected in this framework include enacted stigma (experiences of discrimination, referred to in Chapter 4 as 'social rejection'), perceived stigma (perception of stigmatising attitudes), anticipated stigma (expectations that one will experience stigma) and internalised stigma (endorsement of negative beliefs about oneself, referred to in Chapter 4 as 'internalised shame'). Each of these may have an impact on disclosure, social support, mental health, and treatment outcomes. Indeed, enacted stigma following disclosure may deter future disclosure events [17], speaking to the relevance of the feedback loop included in the Disclosure Processes Model described above. Taken together, these frameworks provide an orientation to the conceptual underpinnings of this thesis and a useful point of departure for the remainder of this review.

2.2 Patterns and predictors of disclosure

As described above, disclosure is a complex and fluid process that occurs within relationships. In research and practice, however, disclosure is typically assessed using self-report. Although self-reported disclosure is not necessarily concordant with confirmation of the disclosure act by the person(s) to whom individuals report having disclosed [18], self-report is the most feasible measure. However, the limitations of using self-report to assess disclosure, including limitations related to social desirability bias, should be noted throughout.

2.2.1 Disclosure to at least one person

HIV-infected individuals disclose to differing numbers of person(s). A range of disclosure strategies have been described, including no disclosure, selective disclosure, or disclosure to a wide range of people [19]. Overall, the most common strategy appears to be selective disclosure, with individuals revealing their HIV status to only a few persons [12, 20-23]. Despite the selective nature of disclosure, however, existing literature suggests that most individuals disclose to at least one person [22]. In 11 studies of general adult populations in sub-Saharan Africa, disclosure to at least one person was reported by ≥70% of participants [20, 24-33]. Of note is that only five of these studies included longitudinal data [20, 24, 28, 30, 32] and only four explicitly described how disclosure was operationalised and assessed prior to presenting results [24, 27, 29, 33].

In samples of women accessing PMTCT services, levels of disclosure to one or more persons are similarly high: in a four-country study of women testing HIV-positive in the context of PMTCT in sub-Saharan Africa, 79% of women reported that they generally kept their HIV status secret, although 83% had disclosed to at least one person [11]. Table 2.1 presents a

summary of selected publications reporting the prevalence of disclosure to at least one person in the context of PMTCT. Although most studies report that ≥70% of women disclosed to at least one person, markedly low levels were reported in Kenya [34] and in an early study in South Africa [35]. Overall, pooled estimates suggest that 67% of pregnant and postpartum women in sub-Saharan Africa disclose to at least one person [36].

Table 2.1 Overview of select sub-Saharan African studies from the past decade reporting the prevalence of disclosure to at least one person in the context of prevention of mother-to-child transmission (PMTCT)

First author; year of publication	Study location	Study population	Used longitudinal data?	Disclosure measure(s) explicitly described in Methods?	Prevalence of disclosure (%)
Ekama; 2012 [37]	Nigeria	Pregnant women attending a PMTCT clinic			87
Ezegwui; 2009 [38]	Nigeria	Women accessing PMTCT services			97
Geubbels; 2018 [39]	Tanzania	Women with a child <18 months old	✓	✓	95
Kirsten; 2011 [40]	Tanzania	Pregnant women initiating combination antiretroviral prophylaxis	✓		97
Lawani; 2014 [41]	Nigeria	Women attending a clinic for infant HIV testing at 18 months postpartum			89
Onono; 2014 [34]	Kenya	Women diagnosed HIV-positive at entry into antenatal care and followed through 4-8 weeks postpartum	✓	✓	31
Ramlagan; 2018 [42]	South Africa	Pregnant women <6 months gestation and with a current partner		✓	72
Visser; 2008 [35]	South Africa	Women diagnosed HIV-positive during the pregnancy		✓	59

Similar to studies among general adult populations, Table 2.1 suggests that most studies describing the prevalence of disclosure to one or more persons are cross-sectional and do not explicitly describe how disclosure was operationalised or assessed prior to presenting results.

2.2.2 Disclosure to sexual partners

Much research has focussed on disclosure to sexual partners, given that disclosure is promoted as a central strategy to reduce transmission of HIV. In general adult populations, the prevalence of disclosure to partner(s) ranges widely, from 49% of adults receiving HIV care in Uganda reporting that they have disclosed to their partner [43], to 85% in Cameroon [44]; other studies from sub-Saharan African report a prevalence between these estimates [31, 45-51]. These differences may reflect underlying characteristics of these relationships, discussed further in Section 2.2.6, below. A recent nationally-representative survey of sexually active adults in South Africa reported that 77% of HIV-infected participants had disclosed to their current sexual partner(s) [52]. Levels of disclosure to partner(s) are significantly lower among women compared to men [3, 53]. In a sample of women in Nigeria, only 24% had disclosed to their partner [54]. An early review of disclosure to sexual partners in developing countries reported that the proportion of women who have disclosed ranges from 17% to 86% [55].

Disclosure to male partners may be particularly difficult among women tested in the context of antenatal care [5]. Pooled estimates from studies among pregnant and postpartum women in sub-Saharan Africa suggest that 64% of women disclose to their male partner(s) [36]. Although some studies have reported that fewer than half of women in the context of PMTCT disclose to their partner [56, 57], higher levels of disclosure have been reported in other studies, summarised in Table 2.2.

Table 2.2 Overview of select sub-Saharan African studies from the past decade reporting the prevalence of disclosure to sexual partner(s) in the context of prevention of mother-to-child transmission (PMTCT)

First author; year of publication	Study location	Study population[1]	Used longitudinal data?	Disclosure measure(s) explicitly described in Methods?	Prevalence of disclosure (%)
Adeniyi; 2017 [58]	South Africa	Immediately postpartum women		✓	74
Brittain; 2015 [59]	South Africa	Pregnant women accessing PMTCT services and reporting a current male partner			74
Bucagu; 2013 [60]	Rwanda	Pregnant women attending a PMTCT clinic	✓	✓	81
Ebuy; 2015 [61]	Ethiopia	Pregnant women on ART >2 months; excluded women on ART before pregnancy			77
Ezegwui; 2009 [38]	Nigeria	Women accessing PMTCT services			91
Kinuthia; 2018 [1]	Kenya	Mothers bringing their infants for 6-week or 9-month immunisations, restricted to women reporting a current male partner			87
Koss; 2017 [62]	Uganda	Previously ART-naïve women who had initiated ART at 12-28 weeks gestation, later contacted to attend one additional study visit (median: 4.2 years after ART initiation)			87
Obai; 2017 [63]	Uganda	Women aged ≥15 years who had delivered at the study clinics	✓	✓	83
Sendo; 2013 [64]	Ethiopia	Pregnant women		✓	73

[1] ART: antiretroviral therapy

Consistent with studies reporting the prevalence of disclosure to at least one person, the majority of the studies included in Table 2.2 are cross-sectional, although more explicitly state that participants were asked to report whether or not they had disclosed their HIV status to their sexual partner(s) prior to reporting results [58, 60, 63, 64].

2.2.3 Disclosure to family members and/or friends

Reported levels of disclosure to family members and/or friends are typically high among adults on ART [65-69]. Of note is that three of these five cited studies were cross-sectional [66-68] and only two explicitly described how disclosure was operationalised and assessed prior to reporting results [66, 68]. Pooled estimates from studies of disclosure among pregnant and postpartum women in sub-Saharan Africa suggest that 40% of women disclose to one or more family members and only 6% to one or more friends [36]. As discussed above, the most common disclosure strategy appears to be selective, rather than widespread, disclosure. Selective disclosure strategies also appear to extend to the targets of disclosure, with some individuals disclosed to more frequently than others. Indeed, the prevalence of disclosure to different individuals varies widely [11, 70-74]. Overall, female family members and friends appear to be the targets of disclosure more frequently compared to males [22, 39, 58, 75-77].

2.2.4 Time to disclosure

Alongside individuals disclosing to different numbers and different categories of people, the timing of first disclosure events after diagnosis may differ widely. Among HIV-infected individuals in Kenya, for example, first reported disclosure events range from within a few hours of diagnosis to several years after diagnosis [78]. Despite this wide range, literature exists to suggest that the majority of first disclosure events occur rapidly after diagnosis. In a

study of adults in South Africa, for example, a high proportion of disclosure events to partners and family members reportedly occurred on the day of diagnosis [17], and the majority of postpartum women in Zimbabwe who disclose their HIV-positive status to their partner reportedly do so within a few days of diagnosis [2]. Other studies from sub-Saharan Africa similarly suggest that most disclosure events occur during the first week or month after diagnosis [50, 57, 79].

2.2.5 Motivations for disclosure

As is evident from the summary above, the prevalence of disclosure to different individuals differs markedly. In addition, the motivations for disclosing to particular individuals differ [80]. Early qualitative research among HIV-infected pregnant women in South Africa suggested that women disclose to their male partners primarily to encourage HIV testing and the reduction of risk behaviours, or out of a sense of obligation; but disclose to relatives and friends because they experience these relationships as supportive [35]. More recent work among postpartum women in South Africa has similarly suggested that women disclose to their male partners out of a sense of duty, and to family members and close friends to gain support [12], where support may include both emotional and practical assistance [81]. Similar findings have been reported among HIV-infected adults in Uganda [71]. Decisions regarding disclosure are additionally based on the individual's perceived trustworthiness and ability to maintain confidentiality, as well as their anticipated reaction to disclosure [21, 82]; indeed, anticipated reactions are a critical consideration in deciding whether to disclose [83, 84].

2.2.6 Determinants of disclosure

Along with differences in motivations, observed determinants of disclosure to different individuals may differ [8, 73], but examining predictors of disclosure to one or more persons

versus disclosure to none will blur these differences. Importantly, predictors of disclosure may vary according to the characteristics of both the HIV-infected individual and the person to whom they may disclose [17]. Among women, a very well-documented predictor of disclosure to a male partner is stable relationship status, for example being married or cohabiting. This association has been observed in multiple diverse contexts [17, 58, 76, 85, 86]. Similarly, decisions to disclose to a sexual partner differ by whether the relationship is casual or committed [83], and the quality of women's relationships with their male partner may be an important factor in deciding whether to disclose [5]. Indeed, non-disclosure may be a marker of an unhealthy relationship [87].

Of concern is that stable relationships may not be the norm in many settings. In Malawi and Uganda, for example, women have described partnerships as being characterised by instability and a lack of trust and communication, with instability potentially heightened by disclosure [88]; similarly, women in South Africa are often in unstable relationships characterised by low expectations of partner commitment and low levels of communication [89, 90]. Women may experience additional difficulties in finding opportunities to disclose when their male partner lives or works far away [74]. Along with unstable relationships being prevalent in South Africa, migrant work is common, further heightening difficulties with disclosure to male partners.

Because women test for HIV at much higher rates than men, for example in the context of antenatal care, women face a disproportionately higher obligation to disclose [90, 91], but there may be substantial gender differences in both the prevalence of and barriers to disclosure [92], with women significantly less likely to disclose to a partner compared to men [17, 27]. Women in many sub-Saharan African countries have described fearing disclosure to

their partners because of the possibilities of abandonment [92, 93] and violence [92, 94]. In some contexts, abandonment after disclosing to their husband would include women losing their social status as a wife [95]. Fears related to disclosing to male partners may be even further heightened in contexts where women are economically dependent on their partners [75, 88, 91, 92, 96]. Indeed, women's fears of abandonment are closely tied to the fear of loss of economic support [55], with economic dependence decreasing the odds of disclosure to male partners among pregnant women [57].

2.2.7 Synthesis

Taken together, the findings summarised above lead to key insights into patterns and predictors of disclosure. Most HIV-infected individuals disclose to at least one person but levels of disclosure to different individuals differ markedly; indeed, selective disclosure appears to be the predominant strategy. The Disclosure Processes Model includes a feedback loop suggesting that one disclosure event can affect subsequent disclosure trajectories, but it has been noted that different disclosure events may not be interchangeable indicators of the same underlying process [8, 9]. The timing of first disclosure events may differ widely but research suggests that most first disclosure events occur rapidly. Disclosure acts may be motivated by approach or avoidance goals; indeed, the motivations for and determinants of disclosure to different people may differ. A well-documented determinant of disclosure to partners is stable relationship status, with major implications in countries such as South Africa where stable relationships may not be the norm. Further, non-disclosure to a partner may be a marker of an unhealthy relationship. Finally, women face a disproportionately high burden to disclose but disclosure to male partners may be particularly difficult for women tested in the context of antenatal care. Indeed, women may delay disclosure to ensure the continuation of social and economic security.

2.3 Interrelated psychosocial issues

2.3.1 HIV-related stigma

Disclosure is closely connected with HIV-related stigma, with stigma described as both affecting and being affected by disclosure [97]. Meta-analyses suggest an inverse relationship [98]: as stigma increases, the likelihood of disclosure decreases. Anticipated stigma, for example, limits levels of disclosure [99, 100] and higher levels of stigma reduce the odds of disclosure [51, 100-102]. Stigma adds to fears about disclosing: individuals fear gossip and blame following disclosure and, in the case of disclosure to a partner, rejection [11, 99]. These fears have led to women testing HIV-positive during pregnancy in Malawi experiencing what they describe as a 'dilemma between silence and openness' [81]. Decreases in stigma and improvements in community attitudes towards HIV have reportedly improved over recent years in some contexts [5, 102, 103], but stigma remains a pervasive issue and a major part of the lives of HIV-infected individuals [6, 22, 88, 104, 105]. Even where individuals have not personally experienced stigma, other forms of stigma may be pervasive, including perceived, anticipated and internalised stigma [21, 85, 99, 106-108].

In addition to affecting disclosure, stigma may have profound negative effects on treatment outcomes. Stigma and discrimination are major challenges to accessing and remaining in care [4, 103, 109-111]. Further along the HIV care cascade, stigma may negatively affect both ART initiation and adherence [95, 112], including in the context of PMTCT [113-115], with a recent systematic review concluding that there is strong evidence for a link between stigma and adherence difficulties [116]. Qualitative research echoes these findings: women cite stigma and inadvertent disclosure as major barriers to participation in PMTCT programmes [117-119] and to adherence [37]. Even where fears of inadvertent disclosure have not

necessarily resulted in suboptimal adherence, these fears have been described as making it challenging to take antiretroviral drugs in the context of PMTCT in South Africa [120].

2.3.2 Social support

Each of disclosure and stigma are strongly interrelated with social support. Indeed, meta-analyses suggest a positive correlation with disclosure and a negative correlation with stigma [98]. Concerns about stigma and the simultaneous need for support contribute to the complexity of decisions about disclosure [19]. As with the associations between disclosure and stigma, however, social support may both affect and be affected by disclosure: individuals are more likely to disclose to person(s) who they perceive as supportive [121] but disclosure may also result in increased support. Among pregnant women, for example, male partners and family members can play an important supportive role following disclosure [115]. Different types of support may stem from disclosure to different individuals, with pregnant and postpartum women in Kenya describing disclosure to a partner as important for emotional and day-to-day support for HIV care and disclosure to family members as a way to ensure future support in the event of their death [6].

Social support is a critical determinant of treatment outcomes. Support from family members, for example, has been identified as improving ART adherence [122]. In the context of PMTCT, social support may be a facilitator of the uptake of antiretrovirals [114], adherence [112, 115], and engagement in care [118]. Improved outcomes may be facilitated through actions such as reminders to take antiretroviral drugs, material support such as food and money, or emotional encouragement and empathy [21, 88]. Receiving social support following disclosure is predicated on a positive response to the disclosure event. Conversely, negative responses to disclosure may lead to both higher levels of stigma and lower levels of

social support [123]. Indeed, initial responses to disclosure and subsequent actions in relation to an individual's HIV status are critical markers of support or the lack thereof [124].

2.3.3 Mental health

Mental health problems are common among people living with HIV globally, including in Africa [125]. Depression is a particularly common mental health problem and is a key outcome in this thesis. In a global survey of HIV-infected adults, for example, 27% of participants reported symptoms of depression [102]. Further, depression may be associated with each of stigma and social support. Observed stigma, or stigma enacted on others in the community, is a major contributor to emotional turmoil [119], and levels of stigma are significantly higher among adults reporting depressive symptoms [102, 126-128]. Conversely, higher levels of depressive symptoms have been found to be associated with low levels of social support [70, 129]. However, there are few considerations of the interrelationships among stigma, social support and depression.

The evidence for an association between depression and disclosure is mixed: some studies have reported that higher levels of depressive symptoms are associated with a lower [85, 129, 130] or higher likelihood of disclosure [70, 102]; others have found no association [131, 132]. One study from the United States demonstrated that the effect of disclosure on depressive symptoms differs depending on the person(s) to whom pregnant women disclose: in this study, disclosure to a male partner by delivery was not associated with postpartum depression, but disclosure to one or more family members was associated with a decreased prevalence of postpartum depression [86]. Depression itself has been highlighted as a major barrier to care and determinant of suboptimal adherence to ART [42, 111, 112, 133]. Further, pregnancy may be a particularly risky period for mental health problems. Pregnancy in the

context of HIV may lead to significant anxiety [134], and women who test HIV-positive during pregnancy may be less prepared to cope with their diagnosis [5].

2.3.4 Unintended pregnancy

An understudied issue in the context of PMTCT is that of unintended pregnancy. The burden of unintended pregnancies globally is massive: reviews report that up to 80 million unintended pregnancies may occur annually [135], with over half of pregnancies among HIV-infected women in sub-Saharan Africa being unintended [136]. Table 2.3 presents data from a selection of cross-sectional studies from sub-Saharan Africa that reported the prevalence of unintended pregnancy among HIV-infected women, unless otherwise specified in the table. All studies report a high burden of unintended pregnancy, with a similar burden reported in the United States [137-139]. Other studies have included measures of ambivalence towards pregnancy: in a study from South Africa, for example, 46% of pregnant HIV-uninfected and HIV-infected women reported that their pregnancy was unintended, and 29% reported ambivalence [140]. Among HIV-uninfected and HIV-infected women in Uganda, mistimed pregnancy was reported by 30% of women, unwanted pregnancy by 13%, and ambivalence by 3% [141]. In a prospective cohort study in South Africa, 62% of pregnancies during one year of follow-up among women on ART were unplanned [142].

Table 2.3 Overview of select recent sub-Saharan African studies reporting the prevalence of unintended pregnancy

First author; year of publication	Study location	Study population[1]	Prevalence of unintended pregnancy (%)
Adeniyi; 2018 [143]	South Africa	Recently postpartum women	71
Feucht; 2014 [144]	South Africa	Mothers of infants born between 2002 and 2009	62
Mayondi; 2016 [145]	Botswana	Pregnant and recently postpartum HIV-uninfected and HIV-infected women	44
O'Shea; 2016 [146]	Malawi	Pregnant women who had initiated ART ≥6 months before the pregnancy	75
Peltzer; 2013 [147]	South Africa	HIV-uninfected and HIV-infected pregnant women	55
Peltzer; 2016 [148]	South Africa	Pregnant women	53
Ramlagan; 2018 [42]	South Africa	Pregnant women accessing PMTCT services	53
Warren; 2013 [149]	Swaziland	Recently postpartum HIV-uninfected and HIV-infected women	69
Woldesenbet; 2015 [150]	South Africa	Nationally-representative survey of mothers attending 6-week immunisation visit	60

[1] All studies include only HIV-infected women unless otherwise specified; ART: antiretroviral therapy; PMTCT: prevention of mother-to-child transmission

.

The psychosocial effects of an unintended pregnancy may be profound. Indeed, an unintended pregnancy causes significant disruption and heightens pre-existing social and economic vulnerabilities [151, 152]. Despite this, there is limited evidence for the impact of an unintended pregnancy on disclosure. Where an unintended pregnancy coincides with a new HIV diagnosis, women have limited time to adjust to both, and qualitative research suggests that some women delay disclosing to their male partner to ensure the continuation of the relationship [151]. Further, unintended pregnancy may be associated with higher levels of depressive symptoms [148], and it has even been suggested that unintended pregnancy may be a risk factor for mother-to-child transmission (MTCT) [153, 154]. However, despite several investigations of the impact of unintended pregnancy on maternal health behaviours and birth outcomes, data on longer-term maternal and child outcomes are lacking [135], particularly in the context of HIV. In addition, pregnancy intentions are nuanced, complex to measure, and change over time [135, 155]. Further, they are influenced by interrelated factors at multiple levels, including the individual, couple, family, and community [155], making causality difficult to determine.

2.3.5 Synthesis

Taken together, stigma, social support, depression and unintended pregnancy are critical constructs that may be related to disclosure and are themselves important factors in PMTCT care. Stigma and social support both affect and are affected by disclosure, and are strongly interrelated; further, each is related to depression. Although levels of stigma have decreased during recent years, it remains pervasive [102, 106, 107]. Depression is prevalent globally, and pregnancy may be a risky period. In particular, a new HIV diagnosis during pregnancy may heighten vulnerability, but the evidence for an association between disclosure and depression is mixed. Finally, unintended pregnancy is prevalent but understudied. Although

the psychosocial impacts are recognised, there is limited evidence for the effect of unintended pregnancy on disclosure and on long-term maternal outcomes in the context of HIV.

2.4 Disclosure and HIV-related outcomes

2.4.1 Impacts along the HIV care cascade

There is widespread interest in the effects of disclosure along the HIV care cascade. In general adult populations and using various measures of disclosure, disclosure has been found to be associated with increased linkage to HIV care [53, 110, 156-158], presentation to care at earlier stages of disease [159], as well as increased likelihood of assessment for ART eligibility and initiation of ART [157]. Following ART initiation, disclosure may improve retention in HIV care [24, 160-162]; the fear of disclosure has been identified as a major barrier to accessing and remaining in care [110]. Disclosure has even been found to be associated with improved CD4 cell response after ART initiation [32, 163] and with reduced mortality [164]. Findings are similar in the context of PMTCT, with non-disclosure highlighted as a major barrier to care in resource-limited settings [111]. Disclosure has been found to be associated with CD4 cell count testing during pregnancy or receiving the result of this test [150], maternal receipt of ART or antiretroviral prophylaxis [165], increased linkage into ongoing HIV care during the postpartum period [166], and a reduced likelihood of disengagement from care [63, 167-169]. Disclosure may even reduce the risk of MTCT, as demonstrated in Kenya [170, 171] and in Rwanda [60], although this association was not observed in Zimbabwe [165].

Alongside potential benefits to outcomes earlier in the care cascade, disclosure may be associated with improved adherence to antiretrovirals and consequent viral suppression. Indeed, non-disclosure has been highlighted as a key determinant of suboptimal adherence to

ART among adults in sub-Saharan Africa [112], and numerous quantitative studies have demonstrated associations between disclosure and improved adherence to ART among pregnant women [115]. The remainder of this section of the review provides a summary of papers reporting associations between disclosure and each of (i) adherence and (ii) viral suppression. As detailed above, literature on the association between disclosure and adherence is included given that this body of work underpins much of the belief that disclosure has beneficial effects on treatment outcomes. The literature on viral suppression then summarises findings using a more objective marker of adherence, and lays the basis for Chapter 7, which explores the effect of disclosure on viral load outcomes.

2.4.2 Impacts on adherence

In general adult populations and using various measures of disclosure, disclosure has been found to be significantly associated with improved adherence based on self-report [25, 67-69, 133, 172], pill count or pharmacy refill [30, 65, 173], or a combination of measures [46, 174, 175] in sub-Saharan African studies. Of note is that only four of these 12 studies included longitudinal data [30, 65, 69, 173] and only three explicitly described how disclosure was operationalised and assessed prior to reporting results [68, 174, 175]. A summary of select papers which report significant associations between disclosure and adherence in the context of PMTCT is presented in Table 2.4, including two studies from South Africa. Overall, the studies suffer from the same methodological limitations as studies reporting associations between disclosure and adherence in general adult populations: most rely on cross-sectional data and self-reported adherence, and few explicitly describe how disclosure was assessed.

Table 2.4 Overview of select sub-Saharan African studies reporting significant associations between disclosure and improved adherence in the context of prevention of mother-to-child transmission (PMTCT)

First author; year of publication	Study location	Study population[1]	Used longitudinal data?	Disclosure measure(s) explicitly described in Methods?	Measure(s) of disclosure	Measure of adherence
Adeniyi; 2018 [176]	South Africa	HIV-infected women who had delivered in selected health centres		✓	Disclosure to (i) partner and (ii) family members	Combination of self-report and pharmacy refill
Ebuy; 2015 [61]	Ethiopia	Pregnant women on ART >2 months; excluded women on ART before pregnancy			Disclosure to a partner	Self-report
Ekama; 2012 [37]	Nigeria	Pregnant women attending a PMTCT clinic			Disclosure to at least one person	Self-report
Kirsten; 2011 [40]	Tanzania	Pregnant women initiating combination antiretroviral prophylaxis	✓		Disclosure to a partner, relative or friend	Medication possession ratio
Kinuthia; 2018 [1]	Kenya	Women bringing their infants for immunisations			Disclosure to a partner	Self-report
Ramlagan; 2018 [42]	South Africa	Pregnant women <6 months gestation and reporting a current partner		✓	Disclosure to at least one person	Self-report

[1] ART: antiretroviral therapy

A notable exception is a study conducted among postpartum women in Zimbabwe: in this study, neither disclosure to a male partner nor disclosure to others was associated with self-reported ingestion of nevirapine (NVP) at the correct time [177]. A further notable exception comes from Kenya, where women diagnosed HIV-positive when entering antenatal care were followed prospectively, with results suggesting that self-reported use of antiretroviral drugs during pregnancy was associated with each of disclosure to (i) anyone, (ii) a male partner and (iii) an immediate family member, but not with disclosure to others, including friends, more distant relatives and members of the community [100]. A study in the context of antenatal care in Malawi which assessed the impact of immediate disclosure, defined as disclosure to a male partner within one day of diagnosis, reported no association with adherence based on pill count [178]. Finally, a particularly notable study investigated the impact of living situations on the association between disclosure and adherence: in this early study of pregnant women offered single-dose NVP in Zambia, disclosure to a male partner was only associated with adherence among women who had delivered at home [179].

2.4.3 Impacts on viral load outcomes

Findings from studies investigating the impact of disclosure on viral load outcomes are more variable. In general adult populations in sub-Saharan Africa and using various measures of disclosure, disclosure has been observed to be associated with improved [28, 68] or poorer viral load outcomes [180]; several studies have found no association between disclosure and viral load outcomes [30, 69, 157]. Consistent with the limitations highlighted throughout this review, only two of these six studies explicitly described how disclosure was operationalised and assessed [68, 157], although most included longitudinal data [28, 30, 69, 157, 180]. In a recent case-control study from South Africa, the odds of virologic failure was higher among adults who had disclosed to their friends or colleagues, compared to their partner or close

relative(s) [181]. Finally, a large multi-country study of women reported no association between viral suppression and disclosure to one or more persons versus disclosure to none [182].

Few studies have explored the impact of disclosure on viral suppression in the context of PMTCT, making this an obvious gap in the literature. A cross-sectional study among recently postpartum women in South Africa reported that disclosure to a sexual partner was associated with a reduced odds of elevated viral load at delivery [58]. Although disclosure to family members was measured in this study, the association with viral load outcomes was not reported. Around four years after ART initiation during pregnancy in Uganda, disclosure to a male partner has been observed to be associated with viral suppression [62]. In this study, the way in which disclosure was operationalised and assessed was not explicitly described. Finally, in a large cohort study of pregnant women in France, non-disclosure to a male partner was found to be significantly associated with elevated viral load at delivery [183].

2.4.4 Causality of associations

The impact of disclosure on adherence and consequent viral suppression may occur in several ways. For example, patients report using a variety of strategies to avoid inadvertent disclosure. Hiding HIV medications is common [6, 21, 92, 184, 185], as is taking antiretrovirals under the guise of medications for other health issues or for pregnancy [21, 186]. However, taking antiretrovirals without having disclosed to household members represents a logistical challenge [187] and may contribute to suboptimal adherence. In addition, individuals may travel to distant clinics to maintain anonymity and avoid inadvertent disclosure [6, 119, 184, 185, 188]. The logistical implications of this strategy may similarly present challenges to engagement in care and consequent challenges to adherence.

Other potential mechanisms of the associations between disclosure and improved outcomes include reduced stigma or increased support [100], or the reaction of the person(s) to whom an individual discloses [113]; each of these possibilities is in line with the conceptual frameworks presented at the beginning of this literature review.

It is important to note the limitations in determining the causality of all associations summarised in this literature review. Disclosure may result directly in assistance with accessing care or may be a marker of more supportive relationships or decreased stigma, both of which may improve engagement in care [156]. Indeed, observed associations between social support and disclosure may be due to disclosure leading to increased support or to individuals disclosing to person(s) who are perceived to be supportive [189]. In line with this, it is plausible that women who disclose to their male partner may be in more supportive relationships compared to those who do not disclose, and that it is these supportive relationships themselves that improve ART adherence [190]. The causality of associations with unintended pregnancy is similarly difficult to determine, as discussed above, given that pregnancy intentions occur within complex individual and social circumstances.

2.5 Discussion

2.5.1 Limitations and research needs

This review provided a summary of existing knowledge related to disclosure as well as four additional constructs of interest: stigma, social support, depression and unintended pregnancy. The limitations of existing knowledge are alluded to above but are expanded on in this section. In particular, limitations pertaining to the three assumptions that this thesis aims to test are summarised below: that (i) disclosure is universally beneficial with (ii) effects that

are consistent over time, and (iii) that these benefits are consistent across the person(s) to whom individuals disclose.

First, there have been few considerations of how the impact of disclosure may differ across context. It has been noted that non-disclosure to a male partner may only negatively affect adherence under certain conditions [113] and that the effect of disclosure may be context- or culture-specific [114]. In line with the viewpoint that non-disclosure may be a marker of an unhealthy relationship, the outcomes of disclosing to male partners may be markers of relationship quality [191]. Without considerations of sub-groups, the assumption that disclosure is universally beneficial cannot be tested, but few studies have explored effects of disclosure within different groups, as is evident from the review above. In addition, it should be noted that exploring the effect of disclosure in contexts where levels of disclosure are extremely high may not be meaningful; indeed, there may not be enough variability in measures of disclosure in these contexts to warrant investigation.

Second, it is clear from the review above that most studies include only cross-sectional data, thus precluding an investigation of the consistency of the effects of disclosure over time. It is notable that associations between disclosure and adherence are less frequently reported in longitudinal compared to cross-sectional studies [192]. Given that disclosure is inherently a dynamic phenomenon that occurs over time, longitudinal research is needed [193]. Alongside this limitation, it was noted in the review above that evidence for the impact of disclosure on viral load is more variable than that for the impact on adherence. As alluded to in Chapter 1, self-reported adherence suffers from social desirability and recall biases. It is plausible that this social desirability bias extends to the reporting of disclosure, such that individuals who report that they have disclosed are also more likely to report optimal adherence.

It has been suggested that the consequences of disclosure to different people may differ [8]. However, evidence for or against the third assumption, that the benefits of disclosure are consistent across the person(s) to whom individuals disclose, is limited given that most research operationalises disclosure as any versus none or focusses on disclosure to one person or category of persons. A recent systematic review of disclosure among pregnant and postpartum women in sub-Saharan Africa reported that 22 of 43 studies operationalised disclosure as any versus none [36]. Further, few authors explicitly describe how disclosure was operationalised and assessed prior to presenting results, as highlighted throughout the review above. It is thus impossible to determine whether the reported measure was the only measure of disclosure assessed, or if the reported measure was the only measure that was significantly associated with the outcome of interest.

Finally, causality is difficult to determine, as alluded to in Section 2.4. First, most existing studies are cross-sectional, as detailed above, and temporality cannot be established. In addition, the potential for confounding cannot be ignored. As summarised above, it is likely that individuals who are in more supportive relationships are more likely to disclose, and that these supportive relationships themselves lead to improved outcomes. Limitations of existing research related to the other constructs of interest in this thesis have been alluded to throughout this review. In particular, there are few considerations of the interrelationships among stigma, social support and depression; mixed evidence for the effect of disclosure on depression; and few considerations of the long-term impacts of unintended pregnancy.

The above limitations lead to several research needs. First, there is a critical need for improved measurement of disclosure. Two notable exceptions to the predominant approach have used psychometric analytic techniques to explore dimensions of disclosure [8, 9]. Given

that patterns of disclosure differ in different contexts, similar explorations in other settings are warranted, and research which explores the effects of disclosure to different individuals is needed. Second, longitudinal data are clearly needed to explore patterns of disclosure as well as the consistency of the effects of disclosure over time, and to ensure the temporality of findings. Third, the impact of disclosure in different sub-groups warrants exploration to provide evidence for or against the assumption that disclosure is universally beneficial. Further, additional research that explores the impact of disclosure on viral load, a robust biological measure and the ultimate goal of ART use, is needed. Finally, quantitative explorations of the interrelationships among stigma, social support and depression; the effect of disclosure on depression; and the long-term impacts of unintended pregnancy are needed.

2.5.2. Context of this thesis

The changing HIV epidemic and treatment guidelines in South Africa have implications for each of the major constructs described above. Indeed, it was noted in Section 2.1 that all of the factors within the socio-ecological framework of ART adherence are situated within a broader social, cultural and political context [7]. South Africa has a complicated history related to HIV and treatment and, despite hopes that increased access to testing and treatment would result in HIV becoming more normalised, levels of stigma remain high in the country [102, 106, 107]. Increased ART availability and uptake has led to HIV becoming a chronic disease, but this has not eliminated the psychological impacts of infection [194]. Indeed, the chronic nature of HIV necessitates a self-management model [195], where disclosure may be an important component of self-management. Disclosure was previously an entry criterion for ART initiation, given the viewpoint that treatment 'buddies' were critical to maintaining optimal adherence [7]. However, this acted as a barrier to treatment initiation, and disclosure is no longer required to initiate ART in the country.

Changes in PMTCT guidelines were summarised in Chapter 1. Early PMTCT regimens included only short-course prophylaxis, but all HIV-infected pregnant and postpartum women are now eligible to initiate lifelong ART under Option B+ guidelines in South Africa. The difficulties of concealing clinic attendance and ART use may be compounded by these guidelines: lifelong care results in many more opportunities for a woman's HIV status to be inadvertently revealed [6]. For women who have not disclosed to individuals in their households, secrecy around ART use is now a lifelong concern. In addition, women now initiate lifelong ART on the day of diagnosis. For women who are newly-diagnosed during pregnancy, there is a need to accept the triple burden of pregnancy, diagnosis and ART eligibility within the very limited time that same-day initiation allows [93, 187]. This has major implications for disclosure, with women in South Africa often reporting that they are not yet ready to disclose but will do so with time [187].

2.5.3 Conclusion

In conclusion, this review has summarised existing knowledge related to HIV-status disclosure as well as four additional constructs of interest: stigma, social support, depression and unintended pregnancy. Overall, the importance of each of these factors in PMTCT care is clear, but existing insights have limitations. In particular, high-quality evidence is needed for the assumptions that (i) disclosure is universally beneficial with (ii) effects that are consistent over time, and (iii) that these benefits are consistent across the person(s) to whom individuals disclose. Using quantitative data, this thesis aims to contribute to the evidence base while addressing some of the limitations inherent in research to date. In particular, this thesis aims to provide insights into the patterns, predictors and impact of disclosure on depression and viral load among pregnant and postpartum women; including considerations of stigma, social support, depression and unintended pregnancy.

References

1. Kinuthia J, Singa B, McGrath CJ, Odeny B, Langat A, Katana A, et al. Prevalence and correlates of non-disclosure of maternal HIV status to male partners: a national survey in Kenya. BMC Public Health. 2018;18:671.
2. Shamu S, Zarowsky C, Shefer T, Temmerman M, Abrahams N. Intimate partner violence after disclosure of HIV test results among pregnant women in Harare, Zimbabwe. PLoS ONE. 2014;9(10):e109447.
3. Bachanas P, Medley A, Pals S, Kidder D, Antelman G, Benech I, et al. Disclosure, knowledge of partner status, and condom use among HIV-positive patients attending clinical care in Tanzania, Kenya, and Namibia. AIDS Patient Care STDS. 2013;27(7):425-435.
4. Iwelunmor J, Ezeanolue EE, Airhihenbuwa CO, Obiefune MC, Ezeanolue CO, Ogedegbe GG. Socio-cultural factors influencing the prevention of mother-to-child transmission of HIV in Nigeria: a synthesis of the literature. BMC Public Health. 2014;14:771.
5. Medley AM, Kennedy CE, Lunyolo S, Sweat MD. Disclosure outcomes, coping strategies, and life changes among women living with HIV in Uganda. Qual Health Res. 2009;19(12):1744-1754.
6. Spangler SA, Abuogi LL, Akama E, Bukusi EA, Helova A, Musoke P, et al. From 'half-dead' to being 'free': resistance to HIV stigma, self-disclosure and support for PMTCT/HIV care among couples living with HIV in Kenya. Cult Health Sex. 2018;20(5):489-503.
7. Norman A, Chopra M, Kadiyala S. Factors related to HIV disclosure in 2 South African communities. Am J Public Health. 2007;97:1775-1781.
8. Dima AL, Stutterheim SE, Lyimo R, de Bruin M. Advancing methodology in the study of HIV status disclosure: the importance of considering disclosure target and intent. Soc Sci Med. 2014;108:166-174.
9. Préau M, Beaulieu-Prévost D, Henry E, Bernier A, Veillette-Bourbeau L, Otis J. HIV serostatus disclosure: development and validation of indicators considering target and modality. Results from a community-based research in 5 countries. Soc Sci Med. 2015;146:137-146.
10. Moses S, Tomlinson M. The fluidity of disclosure: a longitudinal exploration of women's experience and understanding of HIV disclosure in the context of pregnancy and early motherhood. AIDS Care. 2013;25(6):667-675.
11. Hardon A, Vernooij E, Bongololo-Mbera G, Cherutich P, Desclaux A, Kyaddondo D, et al. Women's views on consent, counseling and confidentiality in PMTCT: a mixed-methods study in four African countries. BMC Public Health. 2012;12:26.
12. Hunter-Adams J, Zerbe A, Philips T, Rini Z, Myer L, Petro G, et al. The dimensionality of disclosure of HIV status amongst post-partum women in Cape Town, South Africa. Afr J AIDS Res. 2017;16(2):101-107.
13. Chaudoir SR, Fisher JD. The Disclosure Processes Model: understanding disclosure decision making and postdisclosure outcomes among people living with a concealable stigmatized identity. Psychol Bull. 2010;136(2):236-256.
14. Chaudoir SR, Fisher JD, Simoni JM. Understanding HIV disclosure: a review and application of the Disclosure Processes Model. Soc Sci Med. 2011;72(10):1618-1629.

15. Busza J, Walker D, Hairston A, Gable A, Pitter C, Lee S, et al. Community-based approaches for prevention of mother to child transmission in resource-poor settings: a social ecological review. J Int AIDS Soc. 2012;15(Suppl 2):17373.
16. Turan B, Hatcher AM, Weiser SD, Johnson MO, Rice WS, Turan JM. Framing mechanisms linking HIV-related stigma, adherence to treatment, and health outcomes. Am J Public Health. 2017;107(6):863-869.
17. Abdool Karim Q, Dellar RC, Bearnot B, Werner L, Frohlich JA, Kharsany ABM, et al. HIV-positive status disclosure in patients in care in rural South Africa: implications for scaling up treatment and prevention interventions. AIDS Behav. 2015;19:322-329.
18. Anglewicz P, Chintsanya J. Disclosure of HIV status between spouses in rural Malawi. AIDS Care. 2011;23(8):998-1005.
19. Hult JR, Wrubel J, Bränström R, Acree M, Tedlie Moskowitz J. Disclosure and nondisclosure among people newly diagnosed with HIV: an analysis from a stress and coping perspective. AIDS Patient Care STDS. 2012;26(3):181-190.
20. Vyankandondera J, Mitchell K, Asiimwe-Kateera B, Boer K, Mutwa P, Balinda J-P, et al. Antiretroviral therapy drug adherence in Rwanda: perspectives from patients and healthcare workers using a mixed-methods approach. AIDS Care. 2013;25(12):1504-1512.
21. Watt MH, Maman S, Earp JA, Eng E, Setel PW, Golin CE, et al. "It's all the time in my mind": facilitators of adherence to antiretroviral therapy in a Tanzanian setting. Soc Sci Med. 2009;68:1793-1800.
22. Obermeyer CM, Baijal P, Pegurri E. Facilitating HIV disclosure across diverse settings: a review. Am J Public Health. 2011;101(6):1011-1023.
23. Cataldo F, Chiwaula L, Nkhata M, van Lettow M, Kasende F, Rosenberg NE, et al. Exploring the experiences of women and health care workers in the context of PMTCT Option B Plus in Malawi. J Acquir Immune Defic Syndr. 2017;74:517-522.
24. Akilimali PZ, Musumari PM, Kashala-Abotnes E, Kayembe PK, Lepira FB, Mutombo PB, et al. Disclosure of HIV status and its impact on the loss in the follow-up of HIV-infected patients on potent anti-retroviral therapy programs in a (post-) conflict setting: a retrospective cohort study from Goma, Democratic Republic of Congo. PLoS ONE. 2017;12(2):e0171407.
25. Beyene KA, Gedif T, Gebre-Mariam T, Engidawork E. Highly active antiretroviral therapy adherence and its determinants in selected hospitals from south and central Ethiopia. Pharmacoepidemiol Drug Saf. 2009;18:1007-1015.
26. Dankoli RS, Aliyu AA, Nsubuga P, Nguku P, Ossai OP, Tukur D, et al. HIV disclosure status and factors among adult HIV positive patients in a secondary health facility in north-eastern Nigeria, 2011. Pan Afr Med J. 2014;18(Suppl 1):4.
27. Gadisa T, Tymejczyk O, Gorrell Kulkarni S, Hoffman S, Lahuerta M, Remien RH, et al. Disclosure history among persons initiating antiretroviral treatment at six HIV clinics in Oromia, Ethiopia, 2012-2013. AIDS Behav. 2017;21:70-81.
28. Izudi J, Alioni S, Kerukadho E, Ndungutse D. Virological failure reduced with HIV-serostatus disclosure, extra baseline weight and rising CD4 cells among HIV-positive adults in northwestern Uganda. BMC Infect Dis. 2016;16:614.
29. Longinetti E, Santacatterina M, El-Khatib Z. Gender perspective of risk factors associated with disclosure of HIV status, a cross-sectional study in Soweto, South Africa. PLoS ONE. 2014;9(4):e95440.

30. Ochieng W, Kitawi RC, Nzomo TJ, Mwatelah RS, Kimulwo MJ, Ochieng DJ, et al. Correlates of adherence and treatment failure among Kenyan patients on long-term highly active antiretroviral therapy. J Acquir Immune Defic Syndr. 2015;69:e49-e56.
31. Reda AA, Biadgilign S, Deribe K, Deribew A. HIV-positive status disclosure among men and women receiving antiretroviral treatment in eastern Ethiopia. AIDS Care. 2013;25(8):956-960.
32. Tegegne AS, Ndlovu P, Zewotir T. Determinants of CD4 cell count change and time-to default from HAART; a comparison of separate and joint models. BMC Infect Dis. 2018;18:197.
33. Yonah G, Fredrick F, Leyna G. HIV serostatus disclosure among people living with HIV/AIDS in Mwanza, Tanzania. AIDS Res Ther. 2014;11:5.
34. Onono MA, Cohen CR, Jerop M, Bukusi EA, Turan JM. HIV serostatus and disclosure: implications for infant feeding practice in rural south Nyanza, Kenya. BMC Public Health. 2014;14:390.
35. Visser MJ, Neufeld S, de Villiers A, Makin JD, Forsyth BWC. To tell or not to tell: South African women's disclosure of HIV status during pregnancy. AIDS Care. 2008;20(9):1138-1145.
36. Tam M, Amzel A, Phelps BR. Disclosure of HIV serostatus among pregnant and postpartum women in sub-Saharan Africa: a systematic review. AIDS Care. 2015;27(4):436-450.
37. Ekama SO, Herbertson EC, Addeh EJ, Gab-Okafor CV, Onwujekwe DI, Tayo F, et al. Pattern and determinants of antiretroviral drug adherence among Nigerian pregnant women. J Pregnancy. 2012;2012:851810.
38. Ezegwui HU, Nwogu-Ikojo EE, Enwereji JO, Dim CC. HIV serostatus disclosure pattern among pregnant women in Enugu, Nigeria. J Biosoc Sci. 2009;41:789-798.
39. Geubbels E, Williams A, Ramaiya A, Tancredi D, Young S, Chantry C. HIV status disclosure among postpartum women in rural Tanzania: predictors, experiences and uptake of a nurse-facilitated disclosure intervention. AIDS Care. 2018;30(4):417-425.
40. Kirsten I, Sewangi J, Kunz A, Dugange F, Ziske J, Jordan-Harder B, et al. Adherence to combination prophylaxis for prevention of mother-to-child-transmission of HIV in Tanzania. PLoS ONE. 2011;6(6):e21020.
41. Lawani LO, Onyebuchi AK, Iyoke CA, Onoh RC, Nkwo PO. The challenges of adherence to infant feeding choices in prevention of mother-to-child transmission of HIV infections in south east Nigeria. Patient Prefer Adherence. 2014;8:377-381.
42. Ramlagan S, Peltzer K, Ruiter RAC, Barylski NA, Weiss SM, Sifunda S. Prevalence and factors associated with fixed-dose combination antiretroviral drugs adherence among HIV-positive pregnant women on Option B treatment in Mpumalanga province, South Africa. Int J Environ Res Public Health. 2018;15:161.
43. Osinde MO, Kakaire O, Kaye DK. Factors associated with disclosure of HIV serostatus to sexual partners of patients receiving HIV care in Kabale, Uganda. Int J Gynecol Obstet. 2012;118:61-64.
44. Suzan-Monti M, Blanche J, Bilé P, Koulla-Shiro S, Abu-Zaineh M, Marcellin F, et al. Individual and structural factors associated with HIV status disclosure to main partner in Cameroon: ANRS 12-116 EVAL survey, 2006-2007. J Acquir Immune Defic Syndr. 2011;57:S22-S26.

45. Alemayehu M, Aregay A, Kalayu A, Yebyo H. HIV disclosure to sexual partner and associated factors among women attending ART clinic at Mekelle hospital, northern Ethiopia. BMC Public Health. 2014;14:746.
46. Do NT, Phiri K, Bussmann H, Gaolathe T, Marlink RG, Wester CW. Psychosocial factors affecting medication adherence among HIV-1 infected adults receiving combination antiretroviral therapy (cART) in Botswana. AIDS Res Hum Retroviruses. 2010;26(6):685-691.
47. Fladseth K, Gafos M, Newell ML, McGrath N. The impact of gender norms on condom use among HIV-positive adults in KwaZulu-Natal, South Africa. PLoS ONE. 2015;10(4):e0122671.
48. Genet M, Sebsibie G, Gultie T. Disclosure of HIV seropositive status to sexual partners and its associated factors among patients attending antiretroviral treatment clinic follow up at Mekelle hospital, Ethiopia: a cross sectional study. BMC Res Notes. 2015;8:109.
49. King R, Katuntu D, Lifshay J, Packel L, Batamwita R, Nakayiwa S, et al. Processes and outcomes of HIV serostatus disclosure to sexual partners among people living with HIV in Uganda. AIDS Behav. 2008;12:232-243.
50. Obiri-Yeboah D, Amoako-Sakyi D, Baidoo I, Adu-Oppong A, Rheinländer T. The 'fears' of disclosing HIV status to sexual partners: a mixed methods study in a counseling setting in Ghana. AIDS Behav. 2016;20:126-136.
51. Vu L, Andrinopoulos K, Mathews C, Chopra M, Kendall C, Eisele TP. Disclosure of HIV status to sex partners among HIV-infected men and women in Cape Town, South Africa. AIDS Behav. 2012;16:132-138.
52. Simbayi LC, Zungu N, Evans M, Mehlomakulu V, Kupamupindi T, Mafoko G, et al. HIV serostatus disclosure to sexual partners among sexually active people living with HIV in South Africa: results from the 2012 national population-based household survey. AIDS Behav. 2017;21:82-92.
53. Hatcher AM, Turan JM, Leslie HH, Kanya LW, Kwena Z, Johnson MO, et al. Predictors of linkage to care following community-based HIV counseling and testing in rural Kenya. AIDS Behav. 2012;16:1295-1307.
54. Olowookere SA, Fawole OI, Adekanle DA, Adeleke NA, Abioye-Kuteyi EA. Patterns and correlates of intimate partner violence to women living with HIV/AIDS in Osogbo, southwest Nigeria. Violence Against Women. 2015;21(11):1330-1340.
55. Medley A, Garcia-Moreno C, McGill S, Maman S. Rates, barriers and outcomes of HIV serostatus disclosure among women in developing countries: implications for prevention of mother-to-child transmission programmes. Bull World Health Organ. 2004;82(4):299-307.
56. Brou H, Djohan G, Becquet R, Allou G, Ekouevi DK, Viho I, et al. When do HIV-infected women disclose their HIV status to their male partner and why? A study in a PMTCT programme, Abidjan. PLoS Med. 2007;4(12):e342.
57. Kiula ES, Damian DJ, Msuya SE. Predictors of HIV serostatus disclosure to partners among HIV-positive pregnant women in Morogoro, Tanzania. BMC Public Health. 2013;13:433.
58. Adeniyi OV, Ajayi AI, Selanto-Chairman N, Goon DT, Boon G, Fuentes YO, et al. Demographic, clinical and behavioural determinants of HIV serostatus non-disclosure to sex partners among HIV-infected pregnant women in the Eastern Cape, South Africa. PLoS ONE. 2017;12(8):e0181730.

59. Brittain K, Giddy J, Myer L, Cooper D, Harries J, Stinson K. Pregnant women's experiences of male partner involvement in the context of prevention of mother-to-child transmission in Khayelitsha, South Africa. AIDS Care. 2015;27(8):1020-1024.
60. Bucagu M, Bizimana JDD, Muganda J, Humblet CP. Socio-economic, clinical and biological risk factors for mother-to-child transmission of HIV-1 in Muhima health centre (Rwanda): a prospective cohort study. Arch Public Health. 2013;71:4.
61. Ebuy H, Yebyo H, Alemayehu M. Level of adherence and predictors of adherence to the Option B+ PMTCT programme in Tigray, northern Ethiopia. Int J Infect Dis. 2015;33:123-129.
62. Koss CA, Natureeba P, Kwarisiima D, Ogena M, Clark TD, Olwoch P, et al. Viral suppression and retention in care up to 5 years after initiation of lifelong ART during pregnancy (Option B+) in rural Uganda. J Acquir Immune Defic Syndr. 2017;74:279-284.
63. Obai G, Mubeezi R, Makumbi F. Rate and associated factors of non-retention of mother-baby pairs in HIV care in the elimination of mother-to-child transmission programme, Gulu-Uganda: a cohort study. BMC Health Serv Res. 2017;17:48.
64. Sendo EG, Cherie A, Erku TA. Disclosure experience to partner and its effect on intention to utilize prevention of mother to child transmission service among HIV positive pregnant women attending antenatal care in Addis Ababa, Ethiopia. BMC Public Health. 2013;13:765.
65. Tegegne AS, Ndlovu P, Zewotir T. Factors affecting first month adherence due to antiretroviral therapy among HIV-positive adults at Felege Hiwot teaching and specialized hospital, north-western Ethiopia; a prospective study. BMC Infect Dis. 2018;18:83.
66. Aye WL, Puckpinyo A, Peltzer K. Non-adherence to anti-retroviral therapy among HIV infected adults in Mon State of Myanmar. BMC Public Health. 2017;17:391.
67. Tsega B, Srikanth BA, Shewamene Z. Determinants of non-adherence to antiretroviral therapy in adult hospitalized patients, northwest Ethiopia. Patient Prefer Adherence. 2015;9:373-380.
68. Ramadhani HO, Thielman NM, Landman KZ, Ndosi EM, Gao F, Kirchherr JL, et al. Predictors of incomplete adherence, virologic failure, and antiviral drug resistance among HIV-infected adults receiving antiretroviral therapy in Tanzania. Clin Infect Dis. 2007;45:1492-1498.
69. Bajunirwe F, Arts EJ, Tisch DJ, King CH, Debanne SM, Sethi AK. Adherence and treatment response among HIV-1-infected adults receiving antiretroviral therapy in a rural government hospital in southwestern Uganda. J Int Assoc Physicians AIDS Care. 2009;8(2):139-147.
70. Seth P, Kidder D, Pals S, Parent J, Mbatia R, Chesang K, et al. Psychosocial functioning and depressive symptoms among HIV-positive persons receiving care and treatment in Kenya, Namibia, and Tanzania. Prev Sci. 2014;15:318-328.
71. Ssali SN, Atuyambe L, Tumwine C, Segujja E, Nekesa N, Nannungi A, et al. Reasons for disclosure of HIV status by people living with HIV/AIDS and in HIV care in Uganda: an exploratory study. AIDS Patient Care STDS. 2010;24(10):675-681.
72. Suzan-Monti M, Kouanfack C, Boyer S, Blanche J, Bonono R-C, Delaporte E, et al. Impact of HIV comprehensive care and treatment on serostatus disclosure among Cameroonian patients in rural district hospitals. PLoS ONE. 2013;8(1):e55225.

73. Tsai AC, Bangsberg DR, Kegeles SM, Katz IT, Haberer JE, Muzoora C, et al. Internalized stigma, social distance, and disclosure of HIV seropositivity in rural Uganda. Ann Behav Med. 2013;46:285-294.
74. Kiweewa FM, Bakaki PM, McConnell MS, Musisi M, Namirembe C, Nakayiwa F, et al. A cross-sectional study of the magnitude, barriers, and outcomes of HIV status disclosure among women participating in a perinatal HIV transmission study, "the Nevirapine Repeat Pregnancy study". BMC Public Health. 2015;15:988.
75. Gillett HJ, Parr J. Disclosure among HIV-positive women: the role of HIV/AIDS support groups in rural Kenya. Afr J AIDS Res. 2010;9(4):337-344.
76. Patel R, Ratner J, Gore-Felton C, Kadzirange G, Woelk G, Katzenstein D. HIV disclosure patterns, predictors, and psychosocial correlates among HIV positive women in Zimbabwe. AIDS Care. 2012;24(3):358-368.
77. Naigino R, Makumbi F, Mukose A, Buregyeya E, Arinaitwe J, Musinguzi J, et al. HIV status disclosure and associated outcomes among pregnant women enrolled in antiretroviral therapy in Uganda: a mixed methods study. Reprod Health. 2017;14:107.
78. Miller AN, Rubin DL. Factors leading to self-disclosure of a positive HIV diagnosis in Nairobi, Kenya: people living with HIV/AIDS in the sub-Sahara. Qual Health Res. 2007;17(5):586-598.
79. Roxby AC, Matemo D, Drake AL, Kinuthia J, John-Stewart GC, Ongecha-Owuor F, et al. Pregnant women and disclosure to sexual partners after testing HIV-1-seropositive during antenatal care. AIDS Patient Care STDS. 2013;27(1):33-37.
80. Miller AN, Rubin DL. Motivations and methods for self-disclosure of HIV seropositivity in Nairobi, Kenya. AIDS Behav. 2007;11:687-697.
81. Kasenga F, Hurtig A-K, Emmelin M. HIV-positive women's experiences of a PMTCT programme in rural Malawi. Midwifery. 2010;26:27-37.
82. Poku RA, Owusu AY, Mullen PD, Markham C, McCurdy SA. Considerations for purposeful HIV status disclosure among women living with HIV in Ghana. AIDS Care. 2017;29(5):541-544.
83. Bairan A, Jones Taylor GA, Blake BJ, Akers T, Sowell R, Mendiola R. A model of HIV disclosure: disclosure and types of social relationships. J Am Acad Nurse Pract. 2007;19:242-250.
84. Lugalla J, Yoder S, Sigalla H, Madihi C. Social context of disclosing HIV test results in Tanzania. Cult Health Sex. 2012;14(Suppl 1):S53-S66.
85. Ojikutu BO, Pathak S, Srithanaviboonchai K, Limbada M, Friedman R, Li S, et al. Community cultrual norms, stigma and disclosure to sexual partners among women living with HIV in Thailand, Brazil and Zambia (HPTN 063). PLoS ONE. 2016;11(5):e0153600.
86. Miller ES, Yee LM, Dorman RM, McGregor DV, Sutton SH, Garcia PM, et al. Is maternal disclosure of HIV serostatus associated with a reduced risk of postpartum depression? Am J Obstet Gynecol. 2016;215:521.e1-5.
87. Maman S, Groves AK, McNaughton Reyes HL, Moodley D. Diagnosis and disclosure of HIV status: implications for women's risk of physical partner violence in the postpartum period. J Acquir Immune Defic Syndr. 2014;72:546-551.
88. Flax VL, Yourkavitch J, Okello ES, Kadzandira J, Katahoire AR, Munthali AC. "If my husband leaves me, I will go home and suffer, so better cling to him and hide this

thing": the influence of gender on Option B+ prevention of mother-to-child transmission participation in Malawi and Uganda. PLoS ONE. 2017;12(6):e0178298.

89. Crankshaw TL, Voce A, Butler LM, Darbes L. Expanding the relationship context for couple-based HIV prevention: elucidating women's perspectives on non-traditional sexual partnerships. Soc Sci Med. 2016;166:169-176.
90. Groves AK, Maman S, Moodley D. HIV+ women's narratives of non-disclosure: resisting the label of immorality. Glob Public Health. 2012;7(8):799-811.
91. Bhatia DS, Harrison AD, Kubeka M, Milford C, Kaida A, Bajunirwe F, et al. The role of relationship dynamics and gender inequalities as barriers to HIV-serostatus disclosure: qualitative study among women and men living with HIV in Durban, South Africa. Front Public Health. 2017;5:188.
92. Maeri I, El Ayadi A, Getahun M, Charlebois E, Akatukwasa C, Tumwebaze D, et al. "How can I tell?" Consequences of HIV status disclosure among couples in eastern African communities in the context of an ongoing HIV "test-and-treat" trial. AIDS Care. 2016;28(Suppl 3):59-66.
93. Stinson K, Myer L. Barriers to initiating antiretroviral therapy during pregnancy: a qualitative study of women attending services in Cape Town, South Africa. Afr J AIDS Res. 2012;11(1):65-73.
94. Karamagi CAS, Tumwine JK, Tylleskar T, Heggenhougen K. Intimate partner violence against women in eastern Uganda: implications for HIV prevention. BMC Public Health. 2006;6:284.
95. Carrasco MA, Arias R, Figueroa ME. The multidimensional nature of HIV stigma: evidence from Mozambique. Afr J AIDS Res. 2017;16(1):11-18.
96. Duff P, Kipp W, Wild TC, Rubaale T, Okech-Ojony J. Barriers to accessing highly active antiretroviral therapy by HIV-positive women attending an antenatal clinic in a regional hospital in western Uganda. J Int AIDS Soc. 2010;13:37.
97. Lyimo RA, Stutterheim SE, Hospers HJ, de Glee T, van der Ven A, de Bruin M. Stigma, disclosure, coping, and medication adherence among people living with HIV/AIDS in northern Tanzania. AIDS Patient Care STDS. 2014;28(2):98-105.
98. Smith R, Rossetto K, Peterson BL. A meta-analysis of disclosure of one's HIV-positive status, stigma and social support. AIDS Care. 2008;20(10):1266-1275.
99. Colombini M, Mutemwa R, Kivunaga J, Stackpool Moore L, Mayhew SH, Integra Initiative. Experiences of stigma among women living with HIV attending sexual and reproductive health services in Kenya: a qualitative study. BMC Health Serv Res. 2014;14:412.
100. Spangler SA, Onono M, Bukusi EA, Cohen CR, Turan JM. HIV-positive status disclosure and use of essential PMTCT and maternal health services in rural Kenya. J Acquir Immune Defic Syndr. 2014;67:S235-S242.
101. Przybyla SM, Golin CE, Widman L, Grodensky CA, Earp JA, Suchindran C. Serostatus disclosure to sexual partners among people living with HIV: examining the roles of partner characteristics and stigma. AIDS Care. 2013;25(5):566-572.
102. Nachega JB, Morroni C, Zuniga JM, Sherer R, Beyrer C, Solomon S, et al. HIV-related stigma, isolation, discrimination, and serostatus disclosure: a global survey of 2035 HIV-infected adults. J Int Assoc Physicians AIDS Care. 2012;11(3):172-178.
103. Kulkarni S, Hoffman S, Gadisa T, Melaku Z, Fantehun M, Yigzaw M, et al. Identifying perceived barriers along the HIV care continuum: findings from providers,

peer educators, and observations of provider-patient interactions in Ethiopia. J Int Assoc Provid AIDS Care. 2016;15(4):291-300.

104. Cloete A, Strebel A, Simbayi L, van Wyk B, Henda N, Nqeketo A. Challenges faced by people living with HIV/AIDS in Cape Town, South Africa: issues for group risk reduction interventions. AIDS Res Treat. 2010;2010:420270.
105. Mitzel LD, Vanable PA, Carey MP. HIV-related stigmatization and medication adherence: indirect effects of disclosure concerns and depression. Stigma Health. 2018: Epub ahead of print.
106. dos Santos MML, Kruger P, Mellors SE, Wolvaardt G, van der Ryst E. An exploratory survey measuring stigma and discrimination experienced by people living with HIV/AIDS in South Africa: the People Living with HIV Stigma Index. BMC Public Health. 2014;14:80.
107. Hargreaves JR, Krishnaratne S, Mathema H, Lilleston PS, Sievwright K, Mandla N, et al. Individual and community-level risk factors for HIV stigma in 21 Zambian and South African communities: analysis of data from the HPTN071 (PopART) study. AIDS. 2018;32:783-793.
108. Neuman M, Obermeyer CM, The MATCH Study Group. Experiences of stigma, discrimination, care and support among people living with HIV: a four country study. AIDS Behav. 2013;17:1796-1808.
109. Asghari S, Hurd J, Marshall Z, Maybank A, Hesselbarth L, Hurley O, et al. Challenges with access to healthcare from the perspective of patients living with HIV: a scoping review & framework synthesis. AIDS Care. 2018;30(8):963-972.
110. Govindasamy D, Ford N, Kranzer K. Risk factors, barriers and facilitators for linkage to antiretroviral therapy care: a systematic review. AIDS. 2012;26:2059-2067.
111. O'Hiarlaithe M, Grede N, de Pee S, Bloem M. Economic and social factors are some of the most common barriers preventing women from accessing maternal and newborn child health (MNCH) and prevention of mother-to-child transmission (PMTCT) services: a literature review. AIDS Behav. 2014;18:S516-S530.
112. Heestermans T, Browne JL, Aitken SC, Vervoort SC, Klipstein-Grobusch K. Determinants of adherence to antiretroviral therapy among HIV-positive adults in sub-Saharan Africa: a systematic review. BMJ Glob Health. 2016;1:e000125.
113. Colombini M, Stöckl H, Watts C, Zimmerman C, Agamasu E, Mayhew SH. Factors affecting adherence to short-course ARV prophylaxis for preventing mother-to-child transmission of HIV in sub-Saharan Africa: a review and lessons for future elimination. AIDS Care. 2014;26(7):914-926.
114. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. J Int AIDS Soc. 2013;16:18588.
115. Omonaiye O, Kusljic S, Nicholson P, Manias E. Medication adherence in pregnant women with human immunodeficiency virus receiving antiretroviral therapy in sub-Saharan Africa: a systematic review. BMC Public Health. 2018;18:805.
116. Sweeney SM, Vanable PA. The association of HIV-related stigma to HIV medication adherence: a systematic review and synthesis of the literature. AIDS Behav. 2016;20:29-50.
117. Bwirire LD, Fitzgerald M, Zachariah R, Chikafa V, Massaquoi M, Moens M, et al. Reasons for loss to follow-up among mothers registered in a prevention-of-mother-to-

child transmission program in rural Malawi. Trans R Soc Trop Med Hyg. 2008;102:1195-1200.

118. Chinkonde JR, Sundby J, Martinson F. The prevention of mother-to-child HIV transmission programme in Lilongwe, Malawi: why do so many women drop out. Reprod Health Matters. 2009;17(33):143-151.
119. McMahon SA, Kennedy CE, Winch PJ, Kombe M, Killewo J, Kilewo C. Stigma, facility constraints, and personal disbelief: why women disengage from HIV care during and after pregnancy in Morogoro region, Tanzania. AIDS Behav. 2017;21:317-329.
120. Mepham S, Zondi Z, Mbuyazi A, Mkhwanazi N, Newell ML. Challenges in PMTCT antiretroviral adherence in northern KwaZulu-Natal, South Africa. AIDS Care. 2011;23(6):741-747.
121. Rice E, Comulada S, Green S, Mayfield Arnold E, Rotheram-Borus MJ. Differential disclosure across social network ties among women living with HIV. AIDS Behav. 2009;13:1253-1261.
122. Wasti SP, Simkhada P, Randall J, Freeman JV, van Teijlingen E. Factors influencing adherence to antiretroviral treatment in Nepal: a mixed-methods study. PLoS ONE. 2012;7(5):e35547.
123. Cama E, Brener L, Slavin S, de Wit J. The relationship between negative responses to HIV status disclosure and psychosocial outcomes among people living with HIV. J Health Psychol. 2017: Epub ahead of print.
124. Flax VL, Hamela G, Mofolo I, Hosseinipour MC, Hoffman IF, Maman S. Factors influencing postnatal Option B+ participation and breastfeeding duration among HIV-positive women in Lilongwe district, Malawi: a qualitative study. PLoS ONE. 2017;12(4):e0175590.
125. Brandt R. The mental health of people living with HIV/AIDS in Africa: a systematic review. Afr J AIDS Res. 2009;8(2):123-133.
126. Chan BT, Pradeep A, Prasad L, Murugesan V, Chandrasekaran E, Kumarasamy N, et al. Association between internalized stigma and depression among HIV-positive persons entering into care in southern India. J Glob Health. 2017;7(2):020403.
127. Onyebuchi-Iwudibia O, Brown A. HIV and depression in eastern Nigeria: the role of HIV-related stigma. AIDS Care. 2014;26(5):653-657.
128. Steward WT, Chandy S, Singh G, Panicker ST, Osmand TA, Heylen E, et al. Depression is not an inevitable outcome of disclosure avoidance: HIV stigma and mental health in a cohort of HIV infected individuals from southern India. Psychol Health Med. 2011;16(1):74-85.
129. Vyavaharkar M, Moneyham L, Corwin S, Tavakoli A, Saunders R, Annang L. HIV-disclosure, social support, and depression among HIV-infected African American women living in the rural southeastern United States. AIDS Educ Prev. 2011;23(1):78-90.
130. Yu Y, Luo D, Chen X, Huang Z, Wang M, Xiao S. Medication adherence to antiretroviral therapy among newly treated people living with HIV. BMC Public Health. 2018;18:825.
131. Daskalopoulou M, Lampe FC, Sherr L, Phillips AN, Johnson MA, Gilson R, et al. Non-disclosure of HIV status and associations with psychological factors, ART non-adherence, and viral load non-suppression among people living with HIV in the UK. AIDS Behav. 2017;21:184-195.

132. Mello VA, Segurado AA, Malbergier A. Depression in women living with HIV: clinical and psychosocial correlates. Arch Womens Ment Health. 2010;13:193-199.
133. Letta S, Demissie A, Oljira L, Dessie Y. Factors associated with adherence to antiretroviral therapy (ART) among adult people living with HIV and attending their clinical care, eastern Ethiopia. BMC Int Health Hum Rights. 2015;15:33.
134. Ashaba S, Kaida A, Coleman JN, Burns BF, Dunkley E, O'Neil K, et al. Psychosocial challenges facing women living with HIV during the perinatal period in rural Uganda. PLoS ONE. 2017;12(5):e0176256.
135. Tsui AO, McDonald-Mosley R, Burke AE. Family planning and the burden of unintended pregnancies. Epidemiol Rev. 2010;32:152-174.
136. Feyissa TR, Harris ML, Melka AS, Loxton D. Unintended pregnancy in women living with HIV in sub-Saharan Africa: a systematic review and meta-analysis. AIDS Behav. 2018: Epub ahead of print.
137. Rahangdale L, Stewart A, Stewart RD, Badell M, Levison J, Ellis P, et al. Pregnancy intentions among women living with HIV in the United States. J Acquir Immune Defic Syndr. 2014;65:306-311.
138. Sutton MY, Patel R, Frazier EL. Unplanned pregnancies among HIV-infected women in care - United States. J Acquir Immune Defic Syndr. 2014;65:350-358.
139. Sutton MY, Zhou W, Frazier EL. Unplanned pregnancies and contraceptive use among HIV- positive women in care. PLoS ONE. 2018;13(5):e0197216.
140. Iyun V, Brittain K, Phillips TK, le Roux S, Mcintyre JA, Zerbe A, et al. Prevalence and determinants of unplanned pregnancy in HIV-positive and HIV-negative pregnant women in Cape Town, South Africa: a cross-sectional study. BMJ Open. 2018;8:e019979.
141. Grilo SA, Song X, Lutalo T, Mullinax M, Mathur S, Santelli J. Facing HIV infection and unintended pregnancy: Rakai, Uganda, 2001-2013. BMC Womens Health. 2018;18(1):46.
142. Schwartz SR, Rees H, Mehta S, Venter WDF, Taha TE, Black V. High incidence of unplanned pregnancy after antiretroviral therapy initiation: findings from a prospective cohort study in South Africa. PLoS ONE. 2012;7(4):e36039.
143. Adeniyi OV, Ajayi AI, Moyaki MG, Goon DT, Avramovic G, Lambert J. High rate of unplanned pregnancy in the context of integrated family planning and HIV care services in South Africa. BMC Health Serv Res. 2018;18(1):140.
144. Feucht UD, Meyer A, Kruger M. Missing HIV prevention opportunities in South African children - a 7-year review. BMC Public Health. 2014;14:1265.
145. Mayondi GK, Wirth K, Morroni C, Moyo S, Ajibola G, Diseko M, et al. Unintended pregnancy, contraceptive use, and childbearing desires among HIV-infected and HIV-uninfected women in Botswana: across-sectional study. BMC Public Health. 2016;16:44.
146. O'Shea MS, Rosenberg NE, Tang JH, Mukuzunga C, Kaliti S, Mwale M, et al. Reproductive intentions and family planning practices of pregnant HIV-infected Malawian women on antiretroviral therapy. AIDS Care. 2016;28(8):1027-1034.
147. Peltzer K, Mlambo G. Sexual HIV risk behaviour and associated factors among pregnant women in Mpumalanga, South Africa. BMC Pregnancy Childbirth. 2013;13:57.

148. Peltzer K, Rodriguez VJ, Jones D. Prevalence of prenatal depression and associated factors among HIV-positive women in primary care in Mpumalanga province, South Africa. SAHARA J. 2016;13(1):60-67.
149. Warren CE, Abuya T, Askew I, Integra Initiative. Family planning practices and pregnancy intentions among HIV-positive and HIV-negative postpartum women in Swaziland: a cross sectional survey. BMC Pregnancy Childbirth. 2013;13:150.
150. Woldesenbet S, Jackson D, Lombard C, Dinh T-H, Puren A, Sherman G, et al. Missed opportunities along the prevention of mother-to-child transmission services cascade in South Africa: uptake, determinants, and attributable risk (the SAPMTCTE). PLoS ONE. 2015;10(7):e0132425.
151. Crankshaw TL, Voce A, King RL, Giddy J, Sheon NM, Butler LM. Double disclosure bind: complexities of communicating an HIV diagnosis in the context of unintended pregnancy in Durban, South Africa. AIDS Behav. 2014;18:S53-S59.
152. Lewinsohn R, Crankshaw T, Tomlinson M, Gibbs A, Butler L, Smit J. "This baby came up and then he said, "I give up!": The interplay between unintended pregnancy, sexual partnership dynamics and social support and the impact on women's well-being in KwaZulu-Natal, South Africa. Midwifery. 2018;62:29-35.
153. Beyene GA, Dadi LS, Mogas SB. Determinants of HIV infection among children born to mothers on prevention of mother to child transmission program of HIV in Addis Ababa, Ethiopia: a case control study. BMC Infect Dis. 2018;18(1):327.
154. Mnyani CN, Simango A, Murphy J, Chersich M, McIntyre JA. Patient factors to target for elimination of mother-to-child transmission of HIV. Global Health. 2014;10:36.
155. Haberlen SA, Narasimhan M, Beres LK, Kennedy CE. Integration of family planning services into HIV care and treatment services: a systematic review. Stud Fam Plan. 2017;48(2):153-177.
156. Dorward J, Mabuto T, Charalambous S, Fielding KL, Hoffmann CJ. Factors associated with poor linkage to HIV care in South Africa: secondary analysis of data from the Thol'impilo trial. J Acquir Immune Defic Syndr. 2017;76:453-460.
157. Ostermann J, Pence B, Whetten K, Yao J, Itemba D, Maro V, et al. HIV serostatus disclosure in the treatment cascade: evidence from northern Tanzania. AIDS Care. 2015;27(Suppl 1):59-64.
158. Sanga ES, Lerebo W, Mushi AK, Clowes P, Olomi W, Maboko L, et al. Linkage into care among newly diagnosed HIV-positive individuals tested through outreach and facility-based HIV testing models in Mbeya, Tanzania: a prospective mixed-method cohort study. BMJ Open. 2017;7:e013733.
159. Kigozi IM, Dobkin LM, Martin JN, Geng EH, Muyindike W, Emenyonu NI, et al. Late-disease stage at presentation to an HIV clinic in the era of free antiretroviral therapy in sub-Saharan Africa. J Acquir Immune Defic Syndr. 2009;52:280-289.
160. Elopre L, Hook EW, Westfall AO, Zinski A, Mugavero MJ, Turan J, et al. The role of early HIV status disclosure in retention in HIV care. AIDS Patient Care STDS. 2015;29(12):646-650.
161. Kimeu M, Burmen B, Audi B, Adega A, Owuor K, Arodi S, et al. The relationship between adherence to clinic appointments and year-one mortality for newly enrolled HIV infected patients at a regional referral hospital in western Kenya, January 2011-December 2012. AIDS Care. 2016;28(4):409-415.

162. Seifu W, Ali W, Meresa B. Predictors of loss to follow up among adult clients attending antiretroviral treatment at Karamara general hospital, Jigjiga town, eastern Ethiopia, 2015: a retrospective cohort study. BMC Infect Dis. 2018;18:280.
163. Trinh TT, Yatich N, Ngomoa R, McGrath CJ, Richardson BA, Sakr SR, et al. Partner disclosure and early CD4 response among HIV-infected adults initiating antiretroviral treatment in Nairobi Kenya. PLoS ONE. 2016;11(10):e0163594.
164. Holmes CB, Sikazwe I, Sikombe K, Eshun-Wilson I, Czaicki N, Beres LK, et al. Estimated mortality on HIV treatment among active patients and patients lost to follow-up in 4 provinces of Zambia: findings from a multistage sampling-based survey. PLoS Med. 2018;15(1):e1002489.
165. McCoy SI, Buzdugan R, Padian NS, Musarandega R, Engelsmann B, Martz TE, et al. Uptake of services and behaviors in the prevention of mother-to-child HIV transmission cascade in Zimbabwe. J Acquir Immune Defic Syndr. 2015;69:e74-e81.
166. Watson-Jones D, Balira R, Ross DA, Weiss HA, Mabey D. Missed opportunities: poor linkage into ongoing care for HIV-positive pregnant women in Mwanza, Tanzania. PLoS ONE. 2012;7(7):e40091.
167. Hoffman RM, Phiri K, Parent J, Grotts J, Elashoff D, Kawale P, et al. Factors associated with retention in Option B+ in Malawi: a case control study. J Int AIDS Soc. 2017;20:21464.
168. Sarko KA, Blevins M, Ahonkhai AA, Audet CM, Moon TD, Gebi UI, et al. HIV status disclosure, facility-based delivery and postpartum retention of mothers in a prevention clinical trial in rural Nigeria. Int Health. 2017;9:243-251.
169. Schnack A, Rempis E, Decker S, Braun V, Rubaihayo J, Busingye P, et al. Prevention of mother-to-child transmission of HIV in Option B+ era: uptake and adherence during pregnancy in western Uganda. AIDS Patient Care STDS. 2016;30(3):110-118.
170. McGrath CJ, Singa B, Langat A, Kinuthia J, Ronen K, Omolo D, et al. Non-disclosure to male partners and incomplete PMTCT regimens associated with higher risk of mother-to-child HIV transmission: a national survey in Kenya. AIDS Care. 2018;30(6):765-773.
171. Nyandat J, van Rensburg G. Non-disclosure of HIV-positive status to a partner and mother-to-child transmission of HIV: evidence from a case-control study conducted in a rural county in Kenya. S Afr J HIV Med. 2017;18(1):a691.
172. Molla AA, Gelagay AA, Mekonnen HS, Teshome DF. Adherence to antiretroviral therapy and associated factors among HIV positive adults attending care and treatment in University of Gondar referral hospital, northwest Ethiopia. BMC Infect Dis. 2018;18:266.
173. Charurat M, Oyegunle M, Benjamin R, Habib A, Eze E, Ele P, et al. Patient retention and adherence to antiretrovirals in a large antiretroviral therapy program in Nigeria: a longitudinal analysis for risk factors. PLoS ONE. 2010;5(5):e10584.
174. Yaya I, Landoh DE, Saka B, Patchali PM, Wasswa P, Aboubakari A-S, et al. Predictors of adherence to antiretroviral therapy among people living with HIV and AIDS at the regional hospital of Sokodé, Togo. BMC Public Health. 2014;14:1308.
175. Yaya I, Saka B, Landoh DE, Patchali PM, Patassi AA, Aboubakari A-S, et al. HIV status disclosure to sexual partners, among people living with HIV and AIDS on antiretroviral therapy at Sokodé regional hospital, Togo. PLoS ONE. 2015;10(2):e0118157.

176. Adeniyi OV, Ajayi AI, Goon DT, Owolabi EO, Eboh A, Lambert J. Factors affecting adherence to antiretroviral therapy among pregnant women in the Eastern Cape, South Africa. BMC Infect Dis. 2018;18:175.
177. Kuonza LR, Tshuma CD, Shambira GN, Tshimanga M. Non-adherence to the single dose nevirapine regimen for the prevention of mother-to-child transmission of HIV in Bindura town, Zimbabwe: a cross-sectional analytic study. BMC Public Health. 2010;10:218.
178. Wesevich A, Mtande T, Saidi F, Cromwell E, Tweya H, Hosseinipour MC, et al. Role of male partner involvement in ART retention and adherence in Malawi's Option B+ program. AIDS Care. 2017;29(11):1417-1425.
179. Albrecht S, Semrau K, Kasonde P, Sinkala M, Kankasa C, Vwalika C, et al. Predictors of nonadherence to single-dose nevirapine therapy for the prevention of mother-to-child HIV transmission. J Acquir Immune Defic Syndr. 2006;41(1):114-118.
180. Teshome Yimer Y, Yalew AW. Magnitude and predictors of anti-retroviral treatment (ART) failure in private health facilities in Addis Ababa, Ethiopia. PLoS ONE. 2015;10(5):e0126026.
181. Onoya D, Nattey C, Budgell E, van den Berg L, Maskew M, Evans D, et al. Predicting the need for third-line antiretroviral therapy by identifying patients at high risk for failing second-line antiretroviral therapy in South Africa. AIDS Patient Care STDS. 2017;31(5):205-212.
182. Loutfy M, Johnson M, Walmsley S, Samarina A, Vasquez P, Hao-Lan H, et al. The association between HIV disclosure status and perceived barriers to care faced by women living with HIV in Latin America, China, central/eastern Europe, and western Europe/Canada. AIDS Patient Care STDS. 2016;30(9):435-444.
183. Jasseron C, Mandelbrot L, Dollfus C, Trocmé N, Tubiana R, Teglas JP, et al. Non-disclosure of a pregnant woman's HIV status to her partner is associated with non-optimal prevention of mother-to-child transmission. AIDS Behav. 2013;17:488-497.
184. Elwell K. Facilitators and barriers to treatment adherence within PMTCT programs in Malawi. AIDS Care. 2016;28(8):971-975.
185. Gill MM, Umutoni A, Hoffman HJ, Ndatimana D, Ndayisaba GF, Kibitenga S, et al. Understanding antiretroviral treatment adherence among HIV-positive women at four postpartum time intervals: qualitative results from the Kabeho study in Rwanda. AIDS Patient Care STDS. 2017;31(4):153-166.
186. Clouse K, Schwartz S, Van Rie A, Bassett J, Yende N, Pettifor A. "What they wanted was to give birth; nothing else": barriers to retention in Option B+ HIV care among postpartum women in South Africa. J Acquir Immune Defic Syndr. 2014;67:e12-e18.
187. Black S, Zulliger R, Marcus R, Mark D, Myer L, Bekker L-G. Acceptability and challenges of rapid ART initiation among pregnant women in a pilot programme, Cape Town, South Africa. AIDS Care. 2014;26(6):736-741.
188. Lyimo RA, de Bruin M, van den Boogaard J, Hospers HJ, van der Ven A, Mushi D. Determinants of antiretroviral therapy adherence in northern Tanzania: a comprehensive picture from the patient perspective. BMC Public Health. 2012;12:716.
189. Stirratt MJ, Remien RH, Smith A, Copeland OQ, Dolezal C, Krieger D, et al. The role of HIV serostatus disclosure in antiretroviral medication adherence. AIDS Behav. 2006;10:483-493.

190. Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J, et al. A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women PLoS ONE. 2014;9(11):e111421.
191. Irungu E, Chersich MF, Sanon C, Chege R, Gaillard P, Temmerman M, et al. Changes in sexual behaviour among HIV-infected women in west and east Africa in the first 24 months after delivery. AIDS. 2012;26:997-1007.
192. Katz IT, Ryu AE, Onuegbu AG, Psaros C, Weiser SD, Bangsberg DR, et al. Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis. J Int AIDS Soc. 2013;16(Suppl 2):18640.
193. Varga CA, Sherman GG, Jones SA. HIV-disclosure in the context of vertical transmission: HIV-positive mothers in Johannesburg, South Africa. AIDS Care. 2005;18(8):952-960.
194. Remien RH, Mellins CA. Long-term psychosocial challenges for people living with HIV: let's not forget the individual in our global response to the pandemic. AIDS. 2007;21(Suppl 5):S55-S63.
195. Préau M, Laguette V, March L, Rabaud C, Hardel L, Protopopescu C, et al. Discussing HIV status: is it easier after 10 years of antiretroviral treatment? The ANRS CO8 APROCO-COPILOTE Cohort. AIDS Behav. 2017;21:118-128.

Chapter 3: Patterns and predictors of HIV-status disclosure among pregnant women in South Africa: dimensions of disclosure and influence of social and economic circumstances

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Author contributions

KB conceptualised and conducted the analysis, led data interpretation and drafted the manuscript. TP and AZ directed data collection and assisted with data interpretation. EJA and LM conceptualised the study from which these data arise, were responsible for funding, implementation and overall leadership, and assisted with data interpretation. CAM and RHR contributed to study design and assisted with data interpretation. All authors read and approved the final manuscript.

Abstract

HIV-status disclosure may improve psychosocial health and adherence to antiretroviral therapy (ART), but existing insights suffer from methodological limitations. We explored disclosure over time during pregnancy and postpartum among 1347 HIV-positive women in Cape Town. Among 995 women diagnosed HIV-positive before the pregnancy and entering antenatal care (median age: 30 years), 95% had disclosed to ≥1 individual. In Mokken scale analysis, we observed two separate dimensions of disclosure: disclosure to a male partner, and disclosure to family/community members. Among 352 women diagnosed during the pregnancy and initiating ART (median age: 27 years), 61% disclosed to a male partner and 71% to a family/community member by 12 months after diagnosis. Relationship status modified the impact of pregnancy intentions and poverty on disclosure to a male partner. These unique data provide important insights into dimensions of disclosure during pregnancy and postpartum, and suggest that women's social and economic circumstances are central determinants of disclosure.

3.1 Introduction

HIV-status disclosure may have beneficial effects on both psychosocial health and adherence to antiretroviral therapy (ART) among HIV-positive individuals. As a means of accessing social support from family and community networks, disclosure may improve psychological well-being [1] and facilitate the development of effective coping strategies [2]. Non-disclosure has been identified as a barrier to antiretroviral adherence in studies of adults living with HIV [3] and specifically among women in prevention of mother-to-child transmission (PMTCT) programmes [4-6]. This association may be explained by attempts to hide antiretroviral usage so as not to inadvertently disclose, as well as individuals not receiving support for adherence. Given the potential benefits, disclosure is widely encouraged in counselling services for people living with HIV. Despite widespread fears around disclosing [7-9], documented reactions to disclosure are generally positive, with some evidence linking disclosure to sexual risk reduction in sexual partnerships and the ability to seek care openly, although some individuals do experience negative reactions such as anger or rejection [10, 11]. Most HIV-positive individuals typically report having disclosed to at least one person [7, 12-14], although selective disclosure appears to be the norm, with levels of disclosure to different individuals differing markedly [12].

Disclosure has been described as a process of revealing one's HIV status to an increasing number of individuals over time [12]. This process includes a feedback loop where the individual's positive or negative response to the disclosure event results in greater openness and additional future disclosure events or greater concealment, respectively [1]. Inherent in this model is the effect that one disclosure event can have on subsequent disclosure trajectories. A limitation of much disclosure research to date is the reliance on cross-sectional data to evaluate what is inherently a process that occurs over time [1]. A further limitation is

the commonly used approach of operationalising disclosure as any versus no disclosure, or using sum scores to indicate the total number of persons to whom an individual has disclosed [15]. These approaches treat disclosure to different individuals as interchangeable events. Rather, it has been argued that disclosure should be conceptualised as a multi-dimensional process consisting of clusters of disclosure events to different individuals, given that disclosure events are neither interchangeable nor independent [15, 16]. Based on this idea, two recent studies have sought to extend the methodology of disclosure research using psychometric data reduction techniques in general adult HIV-positive populations [15, 16].

Less attention has been paid to the methodology of disclosure research among HIV-positive pregnant and postpartum women. In terms of disclosure, HIV-positive pregnant women differ from non-pregnant adults in important ways: in South Africa and other high-burden settings, women typically test HIV-positive in the context of antenatal care when they may feel healthy, rather than through voluntary counselling and testing or provider-initiated testing in other contexts. In many low- and middle-income country settings, women may be economically dependent on their male partner, with their economic vulnerability heightened by pregnancy and having implications for disclosure to their male partner [17]. Further, they may be at heightened risk of mental health problems such as depression, particularly in low- and middle-income country settings [18, 19], and may consequently require a greater degree of support. Among HIV-positive pregnant women, levels of disclosure to male partners may be particularly low [20-23], especially among women diagnosed in the context of antenatal care [12, 13, 24, 25]. A widely reported predictor of disclosure to a male partner is stable relationship status [7, 20, 23, 26], but there are few considerations of how factors such as relationship status may modify other determinants of disclosure.

Given methodological limitations in operationalising disclosure and the dearth of longitudinal data, high-quality evidence is lacking, and interventions and counselling messaging are based on data with substantial limitations. To address this gap, we explored patterns and predictors of HIV-status disclosure among HIV-positive pregnant women in Cape Town, South Africa. Our objectives were to explore patterns and predictors of disclosure among three analytic populations, each using different analyses: (i) women diagnosed HIV-positive before the pregnancy and entering antenatal care, using cross-sectional analyses and incorporating psychometric data reduction techniques previously used in a study of HIV-positive adults [15], with (ii) descriptive longitudinal analyses in a subset who were followed through pregnancy and postpartum; and (iii) women diagnosed HIV-positive during the pregnancy and followed through pregnancy and postpartum, using longitudinal analyses.

3.2 Methods

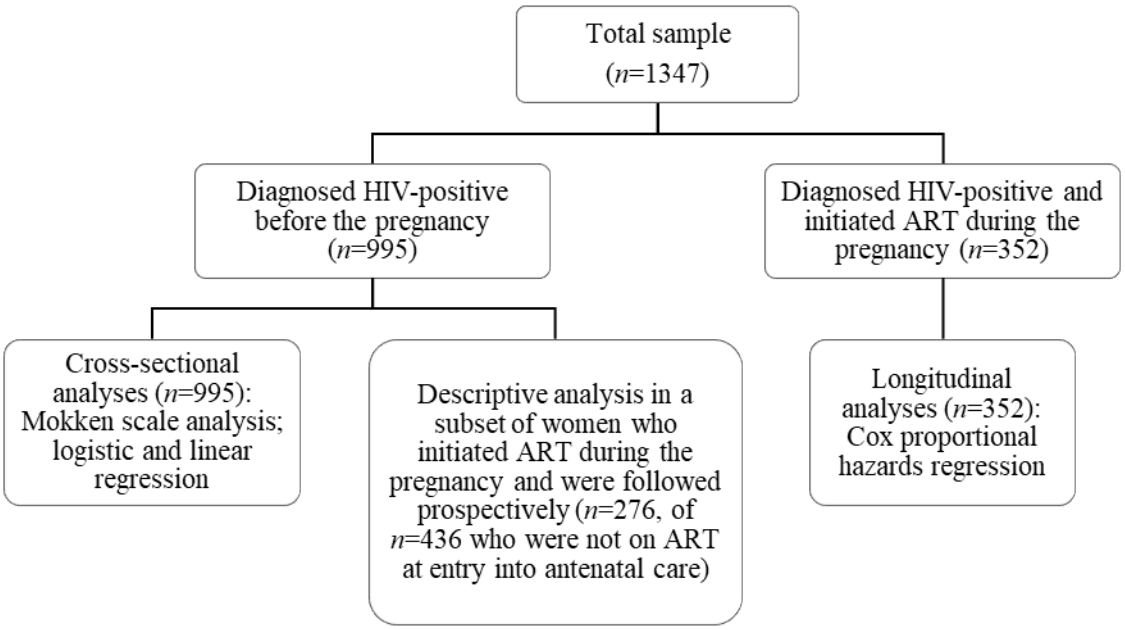
3.2.1 Study design

These secondary analyses draw on the MCH-ART study, a multi-phase implementation science study evaluating strategies for providing HIV care and treatment services in Cape Town (ClinicalTrials.gov NCT01933477). The design and methods of the study have been previously described [27]. The study was conducted at one antenatal care clinic in the former township of Gugulethu, where an antenatal HIV prevalence of ~30% has been documented [28]. In this setting, ART eligibility was determined based on CD4 cell count or clinical disease staging until June 2013; from July 2013 onward, all HIV-positive pregnant women were eligible to initiate lifelong ART under Option B+ guidelines [29].

3.2.2 Participants

For the broader MCH-ART study, consecutive HIV-positive women who were 18 years or older and were entering antenatal care were recruited and enrolled in a cross-sectional evaluation; women who were initiating ART were followed until their first postpartum clinic visit at up to three study visits, with follow-up at up to six additional study visits through 12 months postpartum among women who chose to breastfeed [27]. For the purposes of the current analyses, we used different analytic methods across three analytic populations: (i) a cross-sectional analysis of disclosure reported at entry into antenatal care among all women who were known HIV-positive before the pregnancy; (ii) a descriptive analysis of longitudinal data through 12 months postpartum among women who were known HIV-positive and who were initiating ART and followed as part of the broader study; and (iii) an analysis of longitudinal data through 12 months postpartum among women who were diagnosed HIV-positive during the pregnancy and who were initiating ART and followed as part of the broader study (see Figure 3.1 for an overview of the analytic populations and methods used). All women provided written informed consent prior to enrolment, and the study was approved by the University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee and by Columbia University Medical Center's Institutional Review Board in New York.

Figure 3.1 Analytic populations and methods used[1]



[1] ART: antiretroviral therapy.

3.2.3 Study measures

Study measures were administered in isiXhosa, the predominant local language, by trained interviewers at study visits separate from routine HIV or antenatal/postpartum care. All measures were translated from English into isiXhosa and were back-translated to ensure accuracy using standard procedures for translation and back-translation [30]. Basic sociodemographic characteristics were assessed, and included age, educational attainment and relationship status. Pregnancy intentions were assessed by asking women whether or not they were trying to have a baby when they found out that they were pregnant. A composite poverty score was calculated based on current employment, housing type and access to household assets in order to categorise participants according to relative levels of disadvantage, as previously described [31]. Women self-reported their date of HIV diagnosis, and this was used to calculate the time between diagnosis and entry into antenatal care and to

categorise women according to the timing of diagnosis (before versus during the pregnancy). Gestation was assessed using ultrasound.

Although HIV-status disclosure may be involuntary, for example if someone else reveals the individual's HIV status without his/her permission, only voluntary disclosure was assessed in the broader study, thus we use the term 'disclosure' in the present article to refer only to voluntary disclosure. At entry into antenatal care, disclosure was assessed by asking women whether or not they had told **anyone** that they are HIV-positive, and then by asking whether or not they had disclosed to each of 18 possible categories: male partner; mother; father; sister; brother; daughter; son; uncle; aunt; male cousin; female cousin; other male family member; other female family member; other sexual partner; friend; spiritual leader; current or former employer; and the broader public/community. This list was developed for the purposes of this study, and disclosure to each category was assessed using response options of 'Yes', 'No', or 'Not Applicable'. At each subsequent visit, women were asked whether they had disclosed to anyone new since their last visit, with disclosure to the same 18 possible categories assessed. Given the exploratory nature of these analyses, we combined the response options 'No' and 'Not Applicable' in analyses, and excluded disclosure to certain categories given that disclosure to these categories was infrequently reported: daughter (reported by 9% of women who were diagnosed HIV-positive before the pregnancy), son (6%), employer (4%), other sexual partner (3%) and the public/community (1%).

3.2.4 Data analysis

Data were analysed using Stata 12 (StataCorp Inc, College Station, Texas, USA) and R (R Foundation for Statistical Computing, Austria). Baseline characteristics were summarised

using frequencies and percentages for categorical variables and medians and inter-quartile ranges (IQR) for non-normally distributed variables.

3.2.4.1 Cross-sectional analyses

Among women diagnosed before the pregnancy, we examined the dimensionality of disclosure using Mokken scale analysis, a form of non-parametric item response theory, based on the approach used by Dima et al [15]. The Mokken scale model implies an ordinal scale for observable scores (here, the number of categories of individuals disclosed to), allowing an *ordering of HIV-positive individuals* in terms of the number of categories to whom they report having disclosed [32, 33]. A special case of the model is the double monotonicity model which additionally allows for an *ordering of items* that have invariant item ordering [33]. Here, this would imply that the order in which individuals disclose to different categories does not differ across individuals [34].

Using the *mokken* package in R and the approach recommended by Sijtsma & van der Ark [33], we ran an automated item selection procedure (*aisp*) algorithm 12 times consecutively at increasing values of c (c=0 to c=0.55), where c is a chosen positive coefficient representing the threshold of homogeneity above which an item is included in the scale. We calculated item (H_j, representing how well each item discriminates between individuals' overall disclosure) and total scale (H, representing the accuracy with which items within the total scale are able to order individuals with respect to overall disclosure) scalability coefficients and standard errors; checked scale assumptions; and examined the possibility of invariant item ordering to assess whether or not women disclosed to different categories in the same order. Following this exploratory analysis and based on these results, we examined factors independently associated with disclosure to a male partner and to the sum of

family/community categories (which we refer to as the family/community subscale) in logistic and linear regression models, respectively. As we did not assess the exact number of family/community members to whom women have disclosed (as women may have disclosed to, for example, more than one friend), we used the sum of categories as a proxy for overall disclosure. Finally, we explored factors independently associated with report of any versus no disclosure in logistic regression models in order to serve as a comparison against these more nuanced disclosure analyses. Throughout, we adjusted for sociodemographic characteristics, ART use and time since HIV diagnosis.

3.2.4.2 Longitudinal analyses

Using longitudinal data, we explored the time to first report of disclosure to a male partner and to family/community categories. Where participants reported a new disclosure event at a study visit, we used the midpoint between that and the previous study visit as a proxy for the date of disclosure. Using these data, we then explored the time to first disclosure among previously-diagnosed women who had not disclosed at entry into antenatal care and who initiated ART and were followed prospectively. Similarly, we explored the time to first disclosure among women who were diagnosed during the pregnancy and who initiated ART and were followed prospectively, and used product-limit methods and Cox proportional hazards models to explore variables associated with disclosure to a male partner and to one or more family/community categories. We examined how relationship status may modify the predictors of disclosure to a male partner in stratified analyses by comparing (i) women who were married and/or cohabiting and (ii) women who were neither married nor cohabiting. This latter group included a small number of women who reported that they were not in a relationship.

3.3 Results

3.3.1 Sociodemographic and clinical characteristics

These analyses include data from 1347 HIV-positive pregnant women. A total of 995 pregnant women who were known HIV-positive at entry into antenatal care (median age: 30.5 years) were included in the cross-sectional component, with 276 women who initiated ART during pregnancy and who were followed prospectively included in longitudinal analyses. Longitudinal analyses were also conducted among 352 women who were diagnosed HIV-positive during the pregnancy and initiated ART (median age: 26.9 years). All participants were enrolled between March 2013 and June 2014, and characteristics measured at enrolment are described in Table 3.1. Low levels of educational attainment, employment, and married and/or cohabiting relationship status and high levels of unintended pregnancy were observed in both groups. Among women diagnosed before pregnancy, the median time since HIV diagnosis was 4.2 years.

3.3.2 Reported disclosure at entry into antenatal care among women diagnosed before pregnancy

Among women diagnosed before the pregnancy (n=995, with n=559 on ART at entry into antenatal care), 95% had disclosed to at least one individual, with disclosure to one or more individuals (versus disclosure to none) significantly associated with being on ART at entry into antenatal care (p<0.001) and longer time since HIV diagnosis (p=0.001). No other factors were associated with disclosure to one or more versus no individuals. Disclosure to different categories ranged from 77% of women having disclosed to their male partner, to 9% having disclosed to a spiritual leader; across all categories, disclosure was significantly more common among women who were already on ART when entering antenatal care (Table 3.2).

Table 3.1 Participant characteristics at entry into antenatal care by timing of HIV diagnosis

Variable	Diagnosed before pregnancy – total sample; *n* (%)	Diagnosed before pregnancy – on ART; *n* (%)[1]	Diagnosed before pregnancy – not on ART; *n* (%)	Diagnosed during pregnancy – *n* (%)
Number of women	995	559	436	352
Median [IQR] maternal age	30.5 [26.9, 34.2]	31.5 [27.9, 34.9]	29.4 [26.0, 32.9]	26.9 [23.5, 31.6]
Completed secondary/any tertiary education	233 (23)	125 (22)	108 (25)	109 (31)
Currently employed	353 (35)	212 (38)	141 (32)	146 (41)
Poverty categories				
Least disadvantaged	299 (30)	164 (29)	135 (31)	112 (32)
Moderate disadvantage	329 (33)	191 (34)	138 (32)	116 (33)
Most disadvantaged	367 (37)	204 (36)	163 (37)	124 (35)
Married and/or cohabiting	478 (48)	271 (48)	207 (47)	130 (37)
First pregnancy	88 (9)	58 (10)	30 (7)	95 (27)
Pregnancy unintended	603 (61)	313 (56)	290 (67)	245 (70)
Median [IQR] gestation in weeks	20 [14, 27]	19 [14, 26]	20 [14, 26]	21 [16, 27]
Median [IQR] years since diagnosis	4.2 [2.3, 6.8]	4.6 [2.9, 7.4]	3.7 [1.9, 5.9]	-
On ART	559 (56)	559 (100)	0 (0)	0 (0)

[1] ART: antiretroviral therapy

Table 3.2 Proportion of women reporting having disclosed to different individuals at entry into antenatal care and scalability coefficients (H_j) with standard errors (SE) for the family/community subscale from Mokken scale analysis among 995 women diagnosed HIV-positive before pregnancy

	Proportion of women reporting having disclosed			
	Total sample; *n* (%)	On ART; *n* (%)[1]	Not on ART; *n* (%)	H_j (SE)
Male partner	771 (77)	476 (85)	295 (68)	-
Sister	605 (61)	399 (71)	206 (47)	0.44 (0.03)
Friend	518 (52)	359 (64)	159 (36)	0.39 (0.03)
Mother	471 (47)	303 (54)	168 (39)	0.39 (0.03)
Female cousin	373 (37)	256 (46)	117 (27)	0.54 (0.02)
Brother	372 (37)	266 (48)	106 (24)	0.46 (0.02)
Other female family member	271 (27)	199 (36)	72 (17)	0.57 (0.02)
Male cousin	230 (23)	170 (30)	60 (14)	0.61 (0.02)
Aunt	221 (22)	154 (28)	67 (15)	0.54 (0.02)
Uncle	175 (18)	131 (23)	44 (10)	0.59 (0.02)
Father	164 (16)	114 (20)	50 (11)	0.38 (0.03)
Other male family member	159 (16)	125 (22)	34 (8)	0.62 (0.02)
Spiritual leader	89 (9)	63 (11)	26 (6)	0.45 (0.04)

[1] ART: antiretroviral therapy

Using Mokken scale analysis, we found that disclosure to a male partner formed a separate single-item dimension, while all 12 remaining categories formed one scale. This suggests that the decision to disclose to a male partner in this sample is independent of decisions to disclose to family/community members, with disclosure to family/community categories occurring as related events. Scalability coefficients and standard errors for the 12-item family/community subscale are presented in Table 3.2. For this subscale, H=0.5 (standard error: 0.02), suggesting that these items form a medium-strong scale [35]. The items father, female cousin and other female family member showed signs of violating invariant item ordering, suggesting that these categories are not disclosed to at the same point in the typical order of disclosure events by all women. After exclusion of these categories, the remaining nine items met criteria for invariant item ordering, suggesting that in this sample women tended to disclose to particular categories in the following order: a sister, friend, mother, brother, male cousin, aunt, uncle, other male family member and, lastly, a spiritual leader. This implies that women who had disclosed to, for example, their brother were likely to have also disclosed to their mother, friend and sister. This smaller scale showed medium accuracy

in terms of invariant item ordering (H^T=0.42) and high reliability (Molenaar-Sijtsma coefficient=0.82) [35, 36].

3.3.3 Factors associated with disclosure at entry into antenatal care among women diagnosed before pregnancy

Table 3.3 presents factors associated with disclosure to a male partner, as well as factors associated with the number of categories in the family/community subscale to whom women had disclosed at entry into antenatal care among women diagnosed before the pregnancy. After adjustment for age and time since diagnosis, disclosure to a male partner was strongly associated with being in a married and/or cohabiting relationship [adjusted odds ratio (aOR): 2.51; 95% confidence interval (CI): 1.81, 3.48] and with being on ART at entry into antenatal care (aOR: 2.98; 95% CI: 2.15, 4.11), and was more common among women who had completed secondary or any tertiary education (aOR: 1.59; 95% CI: 1.08, 2.34); no association was observed between length of time since HIV diagnosis and disclosure to a male partner.

As disclosure to family/community categories meets the criteria for a Mokken scale in this sample, sum scores represent a meaningful indicator of disclosure to family/community categories, and allow an ordering of individual women with regard to the number of family/community categories to whom they had disclosed. Women had disclosed to a median of 3 categories (IQR: 1-5) in this subscale. In a multivariable model adjusted for age, the number of categories to whom women had disclosed was lower among women who were in a married and/or cohabiting relationship [regression coefficient (β): -0.95; 95% CI: -1.31, -0.59]. This finding did not differ according to whether or not women had disclosed to their male partner. Other determinants of disclosure to a higher number of family/community

categories were being on ART at entry into antenatal care (β: 1.75; 95% CI: 1.38, 2.12) and a longer time since HIV diagnosis (β for a one-year increase in time since diagnosis: 0.24; 95% CI: 0.18, 0.30). Women who were employed or who reported one or more previous pregnancies had disclosed to fewer family/community categories (β: -0.65; 95% CI: -1.03, -0.27; and β: -0.76; 95% CI: -1.43, -0.09, respectively).

3.3.4 Disclosure over time among women diagnosed before pregnancy

In a subset of 276 women who were diagnosed before the pregnancy but initiated ART during the pregnancy and were followed prospectively, new disclosure events appeared uncommon. Of the 98 women who had not disclosed to their male partner at entry into antenatal care and were followed prospectively, only 25% had disclosed by 12 months after enrolment into the study. Similarly, new disclosure events to family/community categories ranged from 2% of women who had not disclosed at entry into antenatal care disclosing to their father by 12 months after enrolment, to 20% disclosing to a friend.

Table 3.3 Factors associated with disclosure to a male partner and with the number of family/community categories to whom women report having disclosed at entry into antenatal care among 995 women diagnosed HIV-positive before pregnancy

	Disclosure to a male partner				Number of family/community categories			
Variable	Unadjusted OR [95% CI][1]	*P*-value	Adjusted OR [95% CI][2]	*P*-value	Unadjusted β [95% CI][3]	*P*-value	Adjusted β [95% CI][2]	*P*-value
Maternal age	1.00 [0.97, 1.03]	0.791	0.97 [0.94, 1.00]	0.079	0.06 [0.02, 0.10]	0.003	0.01 [-0.04, 0.05]	0.793
Education								
Primary/some secondary	Reference		Reference		Reference			
Secondary/tertiary	1.38 [0.95, 1.99]	0.091	1.59 [1.08, 2.34]	0.018	-0.28 [-0.75, 0.18]	0.236		
Employment								
Unemployed	Reference				Reference		Reference	
Employed	1.12 [0.82, 1.53]	0.478			-0.45 [-0.87, -0.03]	0.031	-0.65 [-1.03, -0.27]	0.001
Poverty categories								
Least disadvantaged	Reference				Reference			
Moderate disadvantage	0.83 [0.57, 1.21]	0.340			-0.21 [-0.71, 0.29]	0.404		
Most disadvantaged	0.99 [0.68, 1.44]	0.970			-0.14 [-0.63, 0.34]	0.562		
Relationship status								
Neither married nor cohabiting	Reference		Reference		Reference		Reference	
Married and/or cohabiting	2.29 [1.67, 3.13]	<0.001	2.51 [1.81, 3.48]	<0.001	-0.89 [-1.28, -0.50]	<0.001	-0.95 [-1.31, -0.59]	<0.001
Previous pregnancies								
First pregnancy	Reference				Reference		Reference	
One or more previous pregnancies	0.81 [0.47, 1.41]	0.453			-0.74 [-1.43, -0.05]	0.037	-0.76 [-1.43, -0.09]	0.027
Antiretroviral therapy (ART) use								
Not on ART	Reference		Reference		Reference		Reference	
On ART	2.74 [2.02, 3.73]	<0.001	2.98 [2.15, 4.11]	<0.001	2.00 [1.62, 3.48]	<0.001	1.75 [1.38, 2.12]	<0.001
Years since diagnosis	1.03 [0.98, 1.07]	0.249	1.01 [0.96, 1.07]	0.585	0.27 [0.21, 0.32]	<0.001	0.24 [0.18, 0.30]	<0.001

[1] OR: odds ratio; 95% CI: 95% confidence interval; [2] Adjusted models are adjusted for covariates shown; [3] β: regression coefficient

3.3.5 Disclosure over time among women diagnosed during pregnancy

The group of 352 women who were diagnosed during the pregnancy and initiated ART were followed for a median of 14.4 months (IQR: 6.1-16.5) from diagnosis. By 12 months after diagnosis, 86% had disclosed to at least one individual. During this time, 61% disclosed to a male partner, and 71% to one or more categories in the family/community subscale, with the frequency of disclosure to each family/community category similar to that observed among women diagnosed before pregnancy. Time to first disclosure events was short: 50% and 53% of women disclosed to their male partner and to a family/community member within 30 days of diagnosis, respectively; with women disclosing to a median of 1 (IQR: 0-2) family/community category over follow-up.

3.3.6 Predictors of disclosure over time among women diagnosed during pregnancy

In unadjusted analyses, disclosure to a male partner was strongly associated with married and/or cohabiting relationship status [hazard ratio (HR): 1.80; 95% CI: 1.37, 2.36] and was more common among women who reported that their pregnancy was intended (HR: 1.45; 95% CI: 1.10, 1.93). In a multivariable Cox proportional hazards model adjusted for poverty, these associations persisted, and disclosing to a male partner was less likely with increasing age [adjusted hazard ratio (aHR): for a one-year increase in age 0.97; 95% CI: 0.95, 1.00]. Marked differences in the predictors of disclosure to a male partner were observed when stratified by relationship status: among women in married and/or cohabiting relationships, intended pregnancy remained significantly associated with disclosure (aHR: 1.61; 95% CI: 1.07, 2.42) after adjustment for age, education, poverty and number of previous pregnancies, but this association was not observed among women who were neither married nor cohabiting (Figure 3.2.1; Figure 3.2.2; Table 3.4). Among this latter group, disclosure to a male partner was less common among those reporting higher levels of poverty (aHR for

moderate disadvantage and most disadvantaged, compared to least disadvantaged: 0.57; 95% CI: 0.37, 0.88; and 0.60; 95% CI: 0.38, 0.97, respectively), independent of age, educational attainment, pregnancy intention and number of previous pregnancies (Figure 3.3.1; Figure 3.3.2; Table 3.4).

Figure 3.2.1 Impact of pregnancy intention on occurrence of disclosure to a male partner among women diagnosed HIV-positive during pregnancy and married and/or cohabiting

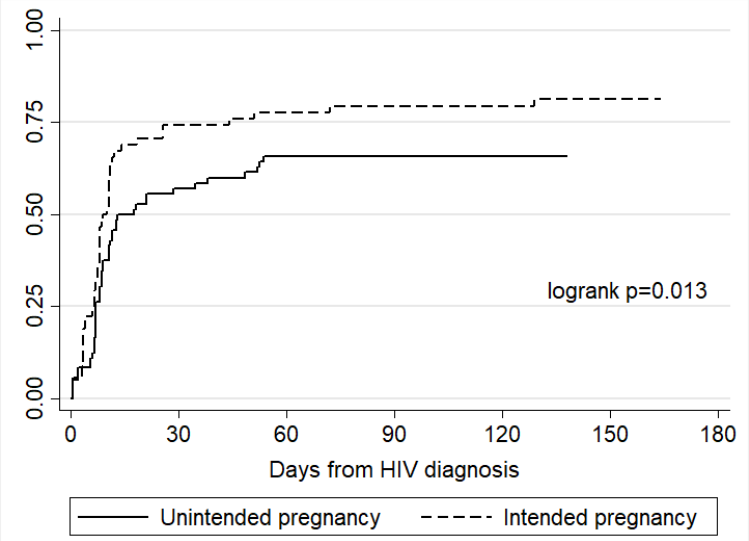


Figure 3.2.2 Impact of pregnancy intention on occurrence of disclosure to a male partner among women diagnosed HIV-positive during pregnancy and neither married nor cohabiting

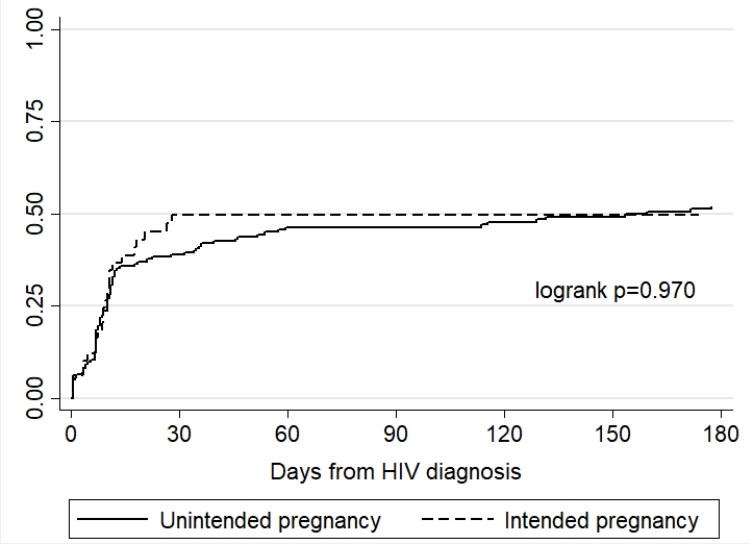


Table 3.4 Impact of relationship status on the predictors of disclosure to a male partner among 352 women diagnosed HIV-positive during pregnancy

	Married and/or cohabiting				Neither married nor cohabiting			
Variable	Unadjusted HR [95% CI][1]	*P*-value	Adjusted HR [95% CI][2]	*P*-value	Unadjusted HR [95% CI]	*P*-value	Adjusted HR [95% CI][2]	*P*-value
Maternal age	0.99 [0.95, 1.03]	0.590	1.00 [0.96, 1.05]	0.835	0.97 [0.93, 1.00]	0.048	0.95 [0.91, 0.99]	0.024
Education								
Primary/some secondary	Reference		Reference		Reference		Reference	
Secondary/tertiary	0.93 [0.59, 1.47]	0.766	0.94 [0.58, 1.52]	0.802	1.52 [1.05, 2.19]	0.028	1.44 [0.98, 2.12]	0.062
Employment								
Unemployed	Reference				Reference			
Employed	0.71 [0.46, 1.09]	0.118			1.03 [0.71, 1.48]	0.886		
Poverty categories								
Least disadvantaged	Reference		Reference		Reference		Reference	
Moderate disadvantage	1.36 [0.77, 2.42]	0.290	1.54 [0.85, 2.80]	0.156	0.55 [0.36, 0.84]	0.006	0.57 [0.37, 0.88]	0.011
Most disadvantaged	1.41 [0.83, 2.37]	0.200	1.46 [0.83, 2.56]	0.189	0.57 [0.36, 0.90]	0.016	0.60 [0.38, 0.97]	0.035
Pregnancy intention								
Unintended	Reference		Reference		Reference		Reference	
Intended	1.64 [1.10, 2.45]	0.016	1.61 [1.07, 2.42]	0.022	1.01 [0.65, 1.57]	0.970	1.02 [0.65, 1.60]	0.946
Previous pregnancies								
First pregnancy	Reference		Reference		Reference		Reference	
One or more previous pregnancies	0.52 [0.31, 0.86]	0.012	0.51 [0.29, 0.90]	0.020	0.89 [0.61, 1.30]	0.531	1.29 [0.81, 2.05]	0.276

[1] HR: hazard ratio; 95% CI: 95% confidence interval; [2] Adjusted models are adjusted for covariates shown

Figure 3.3.1 Impact of poverty on occurrence of disclosure to a male partner among women diagnosed HIV-positive during pregnancy and married and/or cohabiting

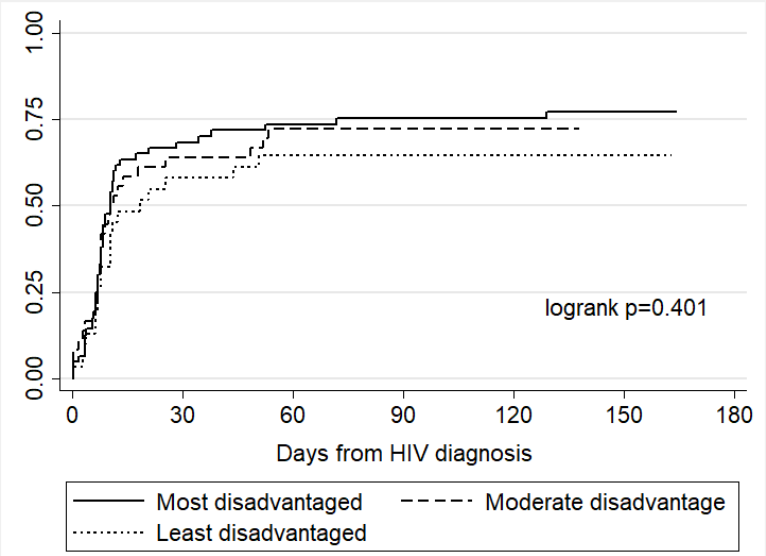
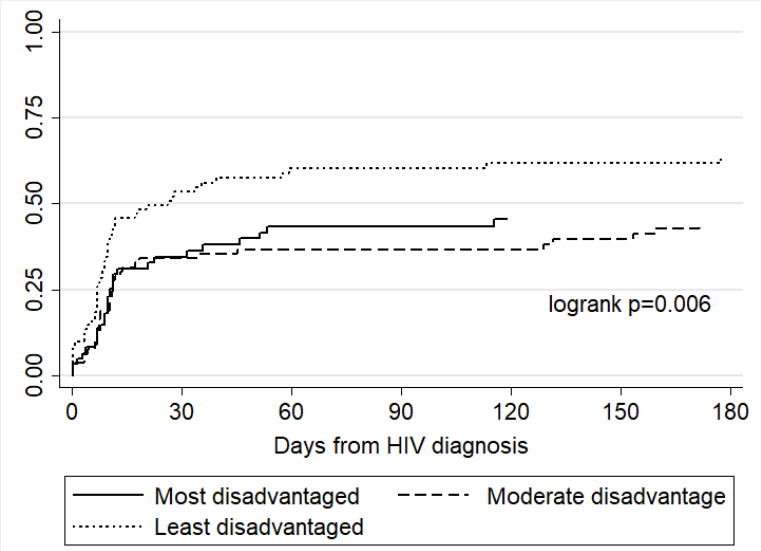


Figure 3.3.2 Impact of poverty on occurrence of disclosure to a male partner among women diagnosed HIV-positive during pregnancy and neither married nor cohabiting



Compared to women who were neither married nor cohabiting, women who were married and/or cohabiting were less likely to disclose to a family/community member over time (HR: 0.62; 95% CI: 0.47, 0.82). This association persisted after adjustment for age and poverty (aHR: 0.62; 95% CI: 0.47, 0.83); no other predictors of disclosure to family/community categories were observed.

3.4 Discussion

This research explored patterns and predictors of disclosure among HIV-positive pregnant women in South Africa. In the group of women diagnosed before the pregnancy, which included both women on ART and women initiating ART during the pregnancy, disclosure appeared to consist of two separate dimensions: disclosure to a male partner, and disclosure to family/community members, with disclosure to family/community categories tending to occur in a particular order. Among women diagnosed during the pregnancy and initiating ART, initial disclosure occurred rapidly but women appeared to favour selective rather than widespread disclosure. Across both groups of women, relationship status was observed to be a central determinant of disclosure, with women who were married and/or cohabiting more likely to disclose to a male partner but less likely to disclose to family/community categories. In addition, relationship status modified the predictors of disclosure to a male partner among women diagnosed during the pregnancy.

3.4.1 Extensions to the literature

This study design and measurements allowed for both cross-sectional and longitudinal insights into a process that inherently occurs over time. Most disclosure research to date has relied solely on cross-sectional data [1], and our longitudinal work notably extends the existing literature. Among women diagnosed before the pregnancy, we showed that time

since diagnosis was associated with disclosure to more family/community categories, but not with disclosure to a male partner. This suggests that women who disclose to their male partner do so quickly, and is consistent with results among newly-diagnosed women: in this group, initial disclosure to male partners and to family/community categories occurred rapidly, as has been observed in a general adult population in South Africa [20].

A further advance introduced by this study is that most research to date operationalises disclosure as any versus no disclosure. Here, we demonstrated in the group of women diagnosed before the pregnancy that operationalising disclosure in this way blurs the predictors of disclosure. Using a novel analytic technique, we showed that disclosure is not a unidimensional process in this sample. Consistent with Dima et al.'s findings [15], we observed that disclosure to a spouse/partner occurs as an independent event. In contrast to their finding of additional disclosure dimensions consisting separately of (i) close family members and (ii) other relatives and the larger community among HIV-positive adults in Tanzania [15], we observed that all family and community categories assessed formed one disclosure subscale. In the present study, we assessed disclosure to individual relatives rather than a single category of 'other relatives', which may have contributed to the differences observed. The single observed scale of disclosure events to family and community categories in the present study may also be due to isiXhosa culture, in which distant or extended family members are often seen to be as close as immediate family members, and nuclear families are relatively uncommon [37]. The order in which women tended to disclose to family/community categories in this sample may reflect the availability of different individuals to provide support, or may be reflective of social distance, again noting that the closeness of family members according to familial relationship may differ in this setting compared to Western settings.

3.4.2 Importance of social and economic circumstances

The finding that married and/or cohabiting relationship status is a central determinant of disclosure to a male partner is well documented [7, 20, 23, 26]. Here, we additionally observed that married and/or cohabiting relationship status is associated with less disclosure to family/community members. We hypothesise that women in married and/or cohabiting relationships may receive a greater degree of support from their male partner, and consequently may experience less need to disclose to other individuals, or that partners may restrict a woman's choice to disclose to family/community members. This finding has important implications for counselling: disclosure is highly dependent on women's social circumstances, and these circumstances need to be taken into account in counselling messages. Conversations about disclosure need to consider the specific life experiences of individual women, as well as individual women's experiences of disclosure.

Further, we observed relationship status to be a modifier of the predictors of male partner disclosure among newly-diagnosed women, again highlighting the importance of context. Compared to women who were married and/or cohabiting, women who were neither married nor cohabiting were significantly less likely to disclose to their male partner, and the intendedness of the pregnancy did not change the likelihood of disclosure in this group. We hypothesise that an unintended pregnancy, which is typically associated with negative outcomes, may have no impact on disclosure when a relationship is already relatively unstable. Previous research in South Africa has suggested that pregnant women's disclosure to their male partner may be subordinated to concerns over maintaining the relationship and receiving continued support [17]. Here, we found that higher levels of poverty were associated with a lower likelihood of disclosure to a male partner among women who were neither married nor cohabiting, suggesting that women who are in less stable relationships

and may be economically dependent on their male partner face heightened vulnerability and may be less likely to disclose. Along these lines, qualitative research in Uganda has highlighted the fear of loss of material and financial support as a key barrier to disclosure to male partners among women who test HIV-positive during antenatal care [38]. Among previously-diagnosed women, the finding that women who had attained higher levels of education were more likely to disclose to their male partner may similarly be explained by higher levels of dependence on their partner among women with lower educational attainment.

3.4.3 Disclosure during pregnancy and postpartum

These data are among the first to explore prospective reports of disclosure among pregnant and postpartum women, a highly vulnerable population. Among women diagnosed during pregnancy, we observed rapid disclosure to both male partners and family/community members, with levels of disclosure broadly similar by 12 months postpartum to levels among women diagnosed before the pregnancy. Although diagnosed during routine HIV testing in the context of antenatal care and clearly influenced by economic and social vulnerabilities, levels of disclosure among newly-diagnosed women were high. However, a better understanding of the differences in disclosure between pregnant and non-pregnant populations is needed, and these findings should be generalised to non-pregnant populations with caution. Further, these findings should be contextualised as arising during a particular period in the HIV epidemic: with dramatically increasing numbers of pregnant women initiating ART, it is possible that HIV and ART have become more normalized over time in this setting, with implications for disclosure. Finally, further study of the impact of disclosure during pregnancy and postpartum is warranted, and longitudinal data are needed to provide high-quality evidence.

3.4.4 Strengths and limitations

A strength of the present study is the inclusion of both cross-sectional and longitudinal data, given the inherent nature of disclosure and the dearth of similar data in the literature, as well as the use of a novel analytic technique to advance understandings of disclosure. In addition, the inclusion of a large sample of HIV-positive women attending primary care increases the generalisability of these findings to other communities of pregnant and postpartum women in the region. A limitation of this analysis is the self-reported nature of these data, given concerns around recall and social desirability bias, although this is common to all disclosure research. Further, we used the first report of disclosure to family/community members in longitudinal analyses, and did not assess the exact number of individuals to whom women have disclosed within categories, thus sum scores in the family/community subscale are only proxies for the total number of disclosure events. Finally, we did not explore the impact of disclosure on HIV or health-related outcomes or on mental health in these analyses.

3.4.5 Conclusion

Despite some limitations, these results provide important insights into disclosure in this population. Our findings suggest that disclosure occurs rapidly after diagnosis but that levels of disclosure to different individuals differ widely, and that disclosure to male partners and family/community members form separate dimensions of disclosure events. Although we ultimately used sum scores as indicators of disclosure to family/community categories, we argue that researchers should first investigate the dimensionality of disclosure events in their data before proceeding with analyses rather than assuming that a rank ordering of individuals is meaningful [32]. Further high-quality evidence of the impact of disclosure on HIV and health-related outcomes is needed in order to inform counselling messaging and intervention efforts, and we argue that basing these on the current evidence base has limitations. Finally,

we note here that women's social and economic circumstances are central determinants of disclosure to both male partners and to family/community members, reflecting women's vulnerability in this context. This suggests that counselling about disclosure needs to consider and be tailored to the broader social and economic circumstances of women's lives, particularly in the case of pregnancy, and that counselling messaging must take into account this vulnerability.

References

1. Chaudoir SR, Fisher JD, Simoni JM. Understanding HIV disclosure: a review and application of the Disclosure Processes Model. Soc Sci Med. 2011;72(10):1618-1629.
2. Medley AM, Kennedy CE, Lunyolo S, Sweat MD. Disclosure outcomes, coping strategies, and life changes among women living with HIV in Uganda. Qual Health Res. 2009;19(12):1744-1754.
3. Govindasamy D, Ford N, Kranzer K. Risk factors, barriers and facilitators for linkage to antiretroviral therapy care: a systematic review. AIDS. 2012;26:2059-2067.
4. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. J Int AIDS Soc. 2013;16:18588.
5. Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J, et al. A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women. PLoS ONE. 2014;9(11):e111421.
6. O'Hiarlaithe M, Grede N, de Pee S, Bloem M. Economic and social factors are some of the most common barriers preventing women from accessing maternal and newborn child health (MNCH) and prevention of mother-to-child transmission (PMTCT) services: a literature review. AIDS Behav. 2014;18:S516-S530.
7. Makin JD, Forsyth BWC, Visser MJ, Sikkema KJ, Neufeld S, Jeffery B. Factors affecting disclosure in South African HIV-positive pregnant women. AIDS Patient Care STDS. 2008;22(11):907-916.
8. Simbayi LC, Kalichman SC, Strebel A, Cloete A, Henda N, Mqeketo A. Disclosure of HIV status to sex partners and sexual risk behaviours among HIV-positive men and women, Cape Town, South Africa. Sex Transm Infect. 2007;83(1):29-34.
9. Vu L, Andrinopoulos K, Mathews C, Chopra M, Kendall C, Eisele TP. Disclosure of HIV status to sex partners among HIV-infected men and women in Cape Town, South Africa. AIDS Behav. 2012;16:132-138.
10. King R, Katuntu D, Lifshay J, Packel L, Batamwita R, Nakayiwa S, et al. Processes and outcomes of HIV serostatus disclosure to sexual partners among people living with HIV in Uganda. AIDS Behav. 2008;12:232-243.
11. Atuyambe LM, Ssegujja E, Ssali S, Tumwine C, Nekesa N, Nannungi A, et al. HIV/AIDS status disclosure increases support, behavioural change and, HIV prevention in the long term: a case for an urban clinic, Kampala, Uganda. BMC Health Serv Res. 2014;14:276.
12. Obermeyer CM, Baijal P, Pegurri E. Facilitating HIV disclosure across diverse settings: a review. Am J Public Health. 2011;101(6):1011-1023.
13. Hardon A, Vernooij E, Bongololo-Mbera G, Cherutich P, Desclaux A, Kyaddondo D, et al. Women's views on consent, counseling and confidentiality in PMTCT: a mixed-methods study in four African countries. BMC Public Health. 2012;12:26.
14. Yonah G, Fredrick F, Leyna G. HIV serostatus disclosure among people living with HIV/AIDS in Mwanza, Tanzania. AIDS Res Ther. 2014;11:5.
15. Dima AL, Stutterheim SE, Lyimo R, de Bruin M. Advancing methodology in the study of HIV status disclosure: the importance of considering disclosure target and intent. Soc Sci Med. 2014;108:166-174.

16. Préau M, Beaulieu-Prévost D, Henry E, Bernier A, Veillette-Bourbeau L, Otis J. HIV serostatus disclosure: development and validation of indicators considering target and modality. Results from a community-based research in 5 countries. Soc Sci Med. 2015;146:137-146.
17. Crankshaw TL, Voce A, King RL, Giddy J, Sheon NM, Butler LM. Double disclosure bind: complexities of communicating an HIV diagnosis in the context of unintended pregnancy in Durban, South Africa. AIDS Behav. 2014;18:S53-S59.
18. Walker SP, Wachs TD, Meeks Gardner J, Lozoff B, Wasserman GA, Pollitt E, et al. Child development: risk factors for adverse outcomes in developing countries. The Lancet. 2007;369(9556):145-157.
19. Walker SP, Wachs TD, Grantham-McGregor S, Black MM, Nelson CA, Huffman SL, et al. Inequality in early childhood: risk and protective factors for early child development. The Lancet. 2011;378(9799):1325-1338.
20. Abdool Karim Q, Dellar RC, Bearnot B, Werner L, Frohlich JA, Kharsany ABM, et al. HIV-positive status disclosure in patients in care in rural South Africa: implications for scaling up treatment and prevention interventions. AIDS Behav. 2015;19:322-329.
21. Genet M, Sebsibie G, Gultie T. Disclosure of HIV seropositive status to sexual partners and its associated factors among patients attending antiretroviral treatment clinic follow up at Mekelle hospital, Ethiopia: a cross sectional study. BMC Res Notes. 2015;8:109.
22. Hardon A, Gomez GB, Vernooij E, Desclaux A, Wanyenze RK, Ky-Zerbo O, et al. Do support groups members disclose less to their partners? The dynamics of HIV disclosure in four African countries. BMC Public Health. 2013;13:589.
23. Obiri-Yeboah D, Amoako-Sakyi D, Baidoo I, Adu-Oppong A, Rheinländer T. The 'fears' of disclosing HIV status to sexual partners: a mixed methods study in a counseling setting in Ghana. AIDS Behav. 2016;20:126-136.
24. Brou H, Djohan G, Becquet R, Allou G, Ekouevi DK, Viho I, et al. When do HIV-infected women disclose their HIV status to their male partner and why? A study in a PMTCT programme, Abidjan. PLoS Med. 2007;4(12):e342.
25. Kiula ES, Damian DJ, Msuya SE. Predictors of HIV serostatus disclosure to partners among HIV-positive pregnant women in Morogoro, Tanzania. BMC Public Health. 2013;13:433.
26. Patel R, Ratner J, Gore-Felton C, Kadzirange G, Woelk G, Katzenstein D. HIV disclosure patterns, predictors, and psychosocial correlates among HIV positive women in Zimbabwe. AIDS Care. 2012;24(3):358-368.
27. Myer L, Phillips TK, Zerbe A, Ronan A, Hsiao N-Y, Mellins CA, et al. Optimizing antiretroviral therapy (ART) for maternal and child health (MCH): rationale and design of the MCH-ART study. J Acquir Immune Defic Syndr. 2016;72:S189-S196.
28. Myer L, Phillips TK, Hsiao N-Y, Zerbe A, Petro G, Bekker L-G, et al. Plasma viraemia in HIV-positive pregnant women entering antenatal care in South Africa. J Int AIDS Soc. 2015;18:20045.
29. Western Cape Government. PMTCT Clinical Guidelines Update, Cape Town, South Africa. Cape Town: Western Cape Government; 2013 [accessed 2016, Jun 29]. Available from: https://www.westerncape.gov.za/assets/departments/health/wcp_2013_pmtct_clinical_guidelines_update_final_replacement_2.pdf

30. Preciago J, Henry H. Linguistic barriers in health education and services. In: Garcia JG, Zea MC, editors. Psychological interventions and research with Latino populations. Boston: Allyn and Bacon; 1997.
31. Brittain K, Mellins CA, Phillips T, Zerbe A, Abrams EJ, Myer L, et al. Social support, stigma and antenatal depression among HIV-infected pregnant women in South Africa. AIDS Behav. 2017;21(1):274-282.
32. Meijer RR, Baneke JJ. Analyzing psychopathology items: a case for nonparametric item response theory modeling. Psychol Methods. 2004;9(3):354-368.
33. Sijtsma K, van der Ark LA. A tutorial on how to do a Mokken scale analysis on your test and questionnaire data. Br J Math Stat Psychol. 2017;70(1):137-158.
34. van Schuur WH. Mokken scale analysis: between the Guttman scale and parametric item response theory. Polit Anal. 2003;11(2):139-163.
35. Stochl J, Jones PB, Croudace TJ. Mokken scale analysis of mental health and well-being questionnaire item responses: a non-parametric IRT method in empirical research for applied health researchers. BMC Med Res Methodol. 2012;12:74.
36. van der Ark LA. New developments in Mokken scale analysis in R. J Stat Softw. 2012;48(5):1-27.
37. South African Department of Social Development. White paper on families in South Africa. Pretoria: South African Department of Social Development; 2012 [accessed 2017, Dec 22]. Available from: http://www.dsd.gov.za/index.php?option=com_docman&task=cat_view&gid=33&Itemid=39
38. Rujumba J, Neema S, Byamugisha R, Tylleskär T, Tumwine JK, Heggenhougen HK. "Telling my husband I have HIV is too heavy to come out of my mouth": pregnant women's disclosure experiences and support needs following antenatal HIV testing in eastern Uganda. J Int AIDS Soc. 2012;15:17429.

Chapter 4: Social support, stigma and antenatal depression among HIV-infected pregnant women in South Africa

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Author contributions

KB conceptualised and conducted the analysis, led data interpretation and drafted the manuscript. TP and AZ directed data collection and assisted with data interpretation. EJA and LM conceptualised the study from which these data arise, were responsible for funding, implementation and overall leadership, and assisted with data interpretation. CAM and RHR contributed to study design and assisted with data interpretation. All authors read and approved the final manuscript.

Abstract

Depression, HIV-related stigma and low levels of social support may be particularly prevalent and adversely affect health and treatment outcomes among HIV-infected pregnant women. We examined factors associated with social support and stigma among pregnant women initiating antiretroviral therapy in the Western Cape, South Africa; and explored associations with depressive symptoms (Edinburgh Postnatal Depression Scale; EPDS) in linear regression models. Among 623 participants, 11 and 19% had elevated EPDS scores using thresholds described in the original development of the scale (scores ≥13 and ≥10, respectively). Social support and stigma were highly interrelated and were associated with depressive symptoms. Stigma was observed to moderate the association between social support and depression scores; when levels of stigma were high, no association between social support and depression scores was observed. Elevated depression scores are prevalent in this setting, and interventions to reduce stigma and to address risk factors for depressive symptoms are needed.

4.1 Background

Antenatal depression is prevalent in low- and middle-income countries (LMICs) [1, 2], with documented adverse effects on both maternal and child health [3-5]. Many of the risk factors for antenatal depression are prevalent in LMIC settings where HIV is most common, including poverty, unplanned pregnancy, and traumatic life events [6]. HIV-infected pregnant women may be a particularly vulnerable group, with high rates of depressive symptoms and psychiatric morbidity reported globally [7]. Other prevalent risk factors in this population may include high levels of HIV-related stigma and low levels of social support, both of which have been shown to have negative effects on factors such as coping [8] and quality of life [9]. Of note is that depression has been shown to be associated with non-adherence to antiretroviral therapy (ART) [10] and with attrition from care [11] in general HIV populations in Africa. Each of depression, HIV-related stigma and a lack of social support have additionally been identified as barriers to accessing prevention of mother-to-child transmission (PMTCT) services [12] and to the uptake of antiretrovirals for PMTCT [13]; and HIV-related stigma is a widely reported barrier to ART initiation, adherence and retention in care among HIV-infected pregnant and postpartum women [14].

There is thus strong evidence that depression and psychosocial factors play an important role in the treatment of HIV disease, and these factors are increasingly understood as constituting barriers to HIV care in the context of both general HIV and PMTCT programmes. In addition, recent evidence suggests that psychosocial factors and depression are interrelated. Studies conducted in sub-Saharan Africa have identified associations between depressive symptoms and both low levels of social support [15] and high levels of HIV-related stigma [16, 17], and recent research conducted among HIV-infected men and women in South Africa has reported that both HIV-related stigma and social support are independently associated

with depression [18]. However, the interrelationships among these constructs are poorly understood, and most previous research has not explored the potentially moderating effect of these factors on the relationships between other factors and depression. Research that simultaneously explores the independent effects of multiple psychosocial factors is needed in order to generate a more nuanced understanding of the complex interrelationships among these constructs, thereby guiding the development of much-needed interventions. Given the well-documented adverse effects of antenatal depression on both maternal and child health and development, and the fact that there are few effective treatment resources for antenatal depression in LMICs [4, 6], this understanding is urgently needed.

Although risk factors for depression have been well described in many populations, including among HIV-infected pregnant women, research into psychosocial factors in the population of women who initiate lifelong ART during pregnancy is needed, as little research has focussed on this population specifically. Although ART eligibility in pregnant women was previously based on CD4 cell count and clinical disease staging, the World Health Organization now recommends that all pregnant women initiate lifelong ART, a recommendation known as 'Option B+' [19]. This recommendation substantially increases the number of ART-eligible pregnant women, and a better understanding of the psychosocial factors that have been shown to impact on HIV care in other populations is needed in this context. We thus examined the factors associated with social support and stigma among HIV-infected pregnant women who were initiating ART in the Western Cape, South Africa; and explored the interrelationships among these constructs and antenatal depressive symptoms. Our aim was (i) to explore variables associated with the perceived availability of social support and HIV-related stigma; and (ii) to explore the relationships between the perceived availability of social support and HIV-related stigma, and antenatal depressive symptoms in this sample.

4.2 Methods

This cross-sectional analysis draws on a multi-phase implementation science study evaluating strategies for delivering HIV care and treatment services during pregnancy and the postpartum period (https://clinicaltrials.gov/ct2/show/NCT01933477). The study is located at a large primary care antenatal clinic in the former township of Gugulethu in Cape Town, South Africa. This stable, low socioeconomic community is characterized by high levels of HIV and poverty, with an antenatal HIV prevalence of 29% [20] and an unemployment rate of 40% [21].

4.2.1 Participants

HIV-infected pregnant women were eligible to participate if they were 18 years or older and were eligible to initiate ART based on current local guidelines during the study period. Between March and June 2013, ART eligibility was determined based on CD4 cell count or clinical staging; after June 2013, all HIV-infected pregnant women were eligible to initiate lifelong ART regardless of CD4 cell count or clinical staging. All women provided written informed consent prior to participation. The study was approved by the University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee and by the Institutional Review Board of the Columbia University Medical Center.

4.2.2 Measures

All measures were translated into isiXhosa, the predominant local language, and were back-translated to ensure accuracy. These measures were piloted prior to the study in order to ensure that items were understood by and applicable to a sample of women recruited from the same population. Given concerns around literacy levels, all measures were administered by trained isiXhosa-speaking interviewers. Study visits were conducted in an interview space

separate from the antenatal clinic at study visits which were scheduled to coincide with participants' routine antenatal visits. Demographic characteristics, including age, marital status, gravidity, and timing of HIV diagnosis, were assessed at participants' first study visit. For our purposes, a composite poverty score was developed in order to categorise participants into tertiles based on their relative level of disadvantage. This composite score was calculated based on current employment status and a standardised composite asset index score based on housing type and household access to a flush toilet, piped water inside the home, electricity, and a refrigerator, telephone and television. Participants were categorised from least to most disadvantaged based on this score.

Participants completed a battery of psychosocial measures at their 2nd antenatal visit, including a 12-item measure to assess the perceived availability of social support. The original measure was constructed as part of the development of methods to identify members of individuals' social support networks, with a view to developing procedures suitable for use in community surveys [22]. This measure was then modified and administered to a sample of HIV-infected injection drug users in the United States, and included domains of both instrumental and emotional support [23]. The measure used in the present study was based on this modified scale. Each item was assessed on a scale ranging from 1 to 5, with higher scores indicating higher levels of social support. The perceived availability of instrumental [Cronbach's alpha (α): 0.88] and emotional support (α: 0.92) were assessed separately by calculating the mean response across items pertaining to these constructs, as widely used elsewhere [24].

HIV-related stigma was assessed using items adapted from the Social Impact Scale [25]. The original scale was developed in order to explore the differential impacts of stigma among

individuals diagnosed with HIV and with cancer, respectively, and was constructed through a process of consultation with clinical experts and HIV-infected individuals as well as factor analysis to group the items into sub-scales [25]. For our purposes, five items from the original scale were included, and two items were added assessing HIV-related stigma in the context of motherhood specifically. Items were assessed on a scale ranging from 1 to 5, with higher scores indicating higher levels of stigma. Mean scores were calculated for items assessing two dimensions of stigma, namely social rejection (α: 0.75) and internalised shame (α: 0.80), as described in the original development of the scale [25].

The Edinburgh Postnatal Depression Scale (EPDS; α: 0.78) [26] was used to measure self-reported symptoms common to depressive disorders. This 10-item measure of recent depressive symptoms was originally developed for use in screening for possible depressive disorders among postnatal women, but has been validated for use in pregnancy [27]. In addition, the scale has been validated for use as a screening tool in South Africa in a sample of postnatal women [28]. Each item of the scale was assessed on a frequency scale ranging from 0 to 3, and a total score was obtained by summing individual item responses, with higher scores indicating more severe depressive symptoms. Threshold values of both ≥10 and ≥13 were explored as suggestive of elevated depressive symptoms, as recommended in the original development of the scale [26]. For our purposes, the EPDS was used as a measure of self-reported depressive symptoms, rather than as a diagnostic tool.

4.2.3 Data analysis

Data were analysed using Stata 12 (StataCorp Inc, College Station, Texas, USA). Variables significantly associated with higher levels of instrumental and emotional support and with higher levels of social rejection and internalised shame were identified using Wilcoxon rank

sum (Mann-Whitney) and Kruskal-Wallis tests. Multivariable linear regression models were built to examine variables independently associated with these constructs. Variables significantly associated with higher depression scores were similarly identified in unadjusted analyses. The associations between social support, stigma, potential confounders, and depressive symptoms were then explored in linear regression models. In order to explore the effects of social support and stigma on depressive symptoms at different levels of the other variable, tertiles of social support and stigma scores were created corresponding to low, medium and high levels. The potentially moderating effect of each variable was then examined graphically at each level of the other variable. Continuous depression scores were used in all analyses, although the proportion of participants with elevated scores on the EPDS was calculated using the suggested threshold values described above.

4.3 Results

4.3.1 Demographic and clinical characteristics and antenatal depressive symptoms

A total of 623 women [median age: 28 years; inter-quartile range (IQR): 24-32], enrolled between March 2013 and April 2014, completed psychosocial measures and were included in the analysis. Detailed demographic and clinical characteristics are presented in Table 4.1. Most participants had not completed secondary education and were currently unemployed, and less than half were married or cohabiting. Most participants reported a previous pregnancy, and most of the current pregnancies were unintended. Just over half of the participants were diagnosed with HIV during the current pregnancy. At the time of their 2nd antenatal visit, 84% of participants had initiated ART, with a median duration of ART use of 16 days (IQR: 14-22). A total of 121 women (19%) had elevated EPDS scores using a threshold of ≥10, and 67 women (11%) had EPDS scores ≥13.

Table 4.1 Demographic and clinical characteristics and antenatal depressive symptoms

Variable	*n* (%)
Number of mothers	623
Age in years – median [IQR]	28 [24, 32]
Ethnicity – Black/African	620 (99.5)
Educational attainment	
Primary/some secondary	457 (73)
Completed secondary/any tertiary	166 (27)
Current employment	
Unemployed	386 (62)
Employed	237 (38)
Poverty level (assets + employment)	
Most disadvantaged	226 (36)
Moderately disadvantaged	205 (33)
Least disadvantaged	192 (31)
Relationship status	
Single	367 (59)
Married/cohabiting	256 (41)
Primigravida	111 (18)
Median gestation in weeks at enrolment [IQR]	20 [16, 26]
Pregnancy intention	
Unintended	439 (70)
Intended	184 (30)
Time of HIV diagnosis	
Before this pregnancy	280 (45)
During this pregnancy	343 (55)
HIV viral load at start of antenatal care	
Median [IQR; $\log_{10}$ copies/mL]	4.0 [3.4, 4.6]
<50 copies/mL	23 (4)
50-1,000 copies/mL	76 (12)
1,001-10,000 copies/mL	216 (35)
10,001-100,000 copies/mL	238 (38)
>100,000 copies/mL	70 (11)
CD4 cell count at start of antenatal care (*n*=607)	
Median [IQR; cells/μL]	343 [235, 507]
≤200 cells/μL	110 (18)
201-350 cells/μL	206 (34)
351-500 cells/μL	135 (22)
>500 cells/μL	156 (26)
Taking antiretroviral therapy (ART) at time of 2nd antenatal visit	524 (84)
Median [IQR] time on ART in days	16 [14, 22]
Antenatal depressive symptoms (EPDS)	
Median score [IQR]	4 [1, 8]
Above threshold ≥10	121 (19)
Above threshold ≥13	67 (11)

4.3.2 Perceived availability of social support

Table 4.2 reports scale scores and item-specific responses from the measures of social support and HIV-related stigma. Although participants reported high levels of social support generally, the reported availability of instrumental support was significantly lower than that of emotional support (mean scores: 4.2 and 4.4, respectively; paired *t* test: t=-6.40; p<0.001). Of note, women reported a low availability of monetary support (mean score for item assessing monetary assistance to pay rent: 3.4). Variables associated with the subscales of social support were examined separately. Higher levels of both social rejection [β: -0.1; 95% confidence interval (CI): -0.2, -0.01; p=0.031] and internalised shame (β: -0.3; 95% CI: -0.4, -0.2; p<0.001) were significantly associated with lower perceived availability of instrumental support, after adjusting for age. In addition, after adjustment for age, participants experiencing higher levels of poverty reported significantly lower availability of instrumental support (β for most versus least disadvantaged: -0.3; 95% CI: -0.4, -0.1; p<0.001), while women who were diagnosed with HIV during the current pregnancy reported higher availability of instrumental support (β: 0.2; 95% CI: 0.03, 0.3; p=0.015). Higher levels of both social rejection (β: -0.2; 95% CI: -0.3, -0.1; p=0.003) and internalised shame (β: -0.2; 95% CI: -0.3, -0.1; p<0.001) were similarly significantly associated with lower perceived availability of emotional support, independent of age and poverty.

Table 4.2 Social support and HIV-related stigma – total scale scores, item-specific responses, and Cronbach's alpha (α) coefficients

Variable	*Mean score (SD)*	α
Perceived availability of support[1]	***4.2 (0.8)***	***0.92***
Instrumental support	*4.2 (0.9)*	*0.88*
Is there someone who would help take care of you if you had to stay in bed for several weeks?	4.4 (1.0)	0.87
Is there someone you could turn to if you needed to borrow R10, get a ride to the doctor, or some other small immediate help?	4.2 (1.2)	0.87
Is there someone you could turn to if you needed to borrow some money to help pay your rent for one month?	3.4 (1.6)	0.91
Is there someone who could take care of your children if you got sick?	4.4 (1.0)	0.87
Is there someone who would help you or be with you when you are having the baby?	4.2 (1.2)	0.87
Is there someone who would help you take care of the baby, after the new baby is born?	4.2 (1.2)	0.87
Is there someone who would help take care of you if you had problems with your pregnancy?	4.4 (1.0)	0.86
Is there someone who would help when you get far along in your pregnancy?	4.4 (1.0)	0.86
Emotional support	*4.4 (0.9)*	*0.92*
Would someone be available to talk to you if you were upset, nervous or depressed?	4.4 (1.0)	0.90
Is there someone you could contact if you wanted to talk about an important personal problem you were having?	4.4 (1.0)	0.89
Would the people in your personal life give you information, suggestions, or guidance if you needed it?	4.3 (1.1)	0.90
Is there someone you could turn to if you needed advice to help make a decision?	4.4 (1.1)	0.90
HIV-related stigma[2]	***2.2 (0.8)***	***0.84***
Social rejection	*1.7 (0.8)*	*0.75*
I feel others are concerned they could "catch" my HIV through contact like a handshake or eating food I make.	1.8 (0.9)	
I feel others avoid me because of my HIV.	1.7 (0.8)	
Internalised shame	*2.4 (0.9)*	*0.80*
I do not feel I can be open with others about my HIV.	2.6 (1.4)	0.70
I feel I need to keep my HIV a secret.	2.6 (1.4)	0.71
Due to my HIV, I have a sense of being unequal in my relationships with others.	1.8 (1.0)	0.79
I feel like I am a bad mother because I am HIV-positive.	1.9 (1.0)	0.76
I worry about who will take care of my baby if I become sick.	2.8 (1.5)	0.82

[1] Items scored between 1 and 5, with higher scores indicating greater perceived availability of support; [2] Items scored between 1 and 5, with higher scores indicating greater stigma

4.3.3 HIV-related stigma

In terms of HIV-related stigma, reported levels of internalised shame were higher than those of social rejection (mean score: 2.4 and 1.7 respectively; paired *t* test: t=-20.77; p<0.001). Women reported the highest levels of stigma on items assessing secrecy around their HIV-infection (mean scores: 2.6 for both items) and on the item assessing concern around who will take care of their baby if they become sick (mean score: 2.8). Correlates of both dimensions of HIV-related stigma were explored separately. After adjustment for age and poverty, increased availability of both instrumental (β: -0.2; 95% CI: -0.3, -0.1; p<0.001) and emotional support (β: -0.1; 95% CI: -0.2, -0.02; p=0.013) were significantly associated with lower reported levels of social rejection. Higher levels of both dimensions of social support were similarly associated with lower levels of internalised shame in unadjusted analyses. In adjusted analyses, the relationship between higher levels of the perceived availability of instrumental support remained significantly associated with lower levels of internalised shame (β: -0.3; 95% CI: -0.5, -0.2; p<0.001), independent of age, poverty, and the perceived availability of emotional support.

4.3.4 Variables associated with antenatal depressive symptoms

The relationships between demographic and psychosocial constructs, and antenatal depressive symptoms were explored. In unadjusted analyses, significantly higher depression scores were observed among mothers who reported single marital status, an unintended pregnancy, and higher levels of social rejection and internalised shame. In addition, increases in age and in the perceived availability of instrumental and emotional support were significantly associated with lower depression scores (Table 4.3). When adjusted for age, marital status and pregnancy intention (adjusted model A), the associations between both dimensions of HIV-related stigma and depression scores persisted, as did the associations between both dimensions of social support and depression scores. In a multivariable model

adjusted for all other covariates (adjusted model B), maternal age, the report of an unintended pregnancy, and higher levels of social rejection and internalised shame remained significantly associated with depression scores, with a stronger effect observed for internalised shame compared to that observed for social rejection. A one-unit increase in social rejection was associated with a 0.7 unit increase (95% CI: 0.1, 1.3; p=0.025) in depression score; compared to a 1.8 unit increase in depression score (95% CI: 1.2, 2.3; p<0.001) associated with a one-unit increase in internalised shame, independent of marital status, pregnancy intention and the perceived availability of both instrumental and emotional support.

When stratified by tertiles of social support, a clear dose-response relationship was observed between tertiles of HIV-related stigma and increasing depression scores across all levels of social support (Figure 4.1.1). In contrast, a clear dose-response relationship was observed between higher levels of perceived social support and lower depression scores only when HIV-related stigma was low (Figure 4.1.2). At higher levels of stigma, the relationship between social support and depressive symptoms did not persist, suggesting that HIV-related stigma moderates the relationship between social support and depressive symptoms. This same moderating effect was observed when the subscales of social support and HIV-related stigma were examined. Specifically, social rejection and internalised shame were observed to moderate the effects of the perceived availability of instrumental and emotional support on depression scores.

Table 4.3 Association between perceived availability of social support, HIV-related stigma, and antenatal depressive symptoms

Variable	Mean EPDS score (SD)	Unadjusted regression coefficient [95% CI]	*P*-value	(A) Regression coefficient [95% CI][1]	*P*-value	(B) Regression coefficient [95% CI][2]	*P*-value
Age		-0.1 [-0.2, -0.002]	0.044			-0.1 [-0.1, -0.01]	0.035
Educational attainment							
Completed secondary/any tertiary	5.2 (5.5)	Reference					
Primary/some secondary	5.3 (5.2)	0.1 [-0.8, 1.1]	0.757				
Current employment							
Employed	4.8 (5.1)	Reference					
Unemployed	5.6 (5.3)	0.8 [-0.03, 1.7]	0.060				
Poverty level							
Least disadvantaged	4.8 (5.0)	Reference					
Moderately disadvantaged	5.2 (5.3)	0.4 [-0.6, 1.5]	0.405				
Most disadvantaged	5.7 (5.4)	0.9 [-0.1, 2.0]	0.066				
Relationship status							
Married/cohabiting	4.7 (4.8)	Reference				Reference	
Single	5.7 (5.5)	1.0 [0.1, 1.8]	0.023			0.6 [-0.2, 1.4]	0.136
Pregnancy intention							
Intended	4.3 (4.6)	Reference				Reference	
Unintended	5.7 (5.5)	1.4 [0.5, 2.3]	0.002			1.0 [0.2, 1.9]	0.018
Time of HIV diagnosis							
Before this pregnancy	5.3 (5.2)	Reference					
During this pregnancy	5.3 (5.3)	0.03 [-0.8, 0.9]	0.949				
Perceived availability of support – instrumental		-1.1 [-1.6, -0.6]	<0.001	-1.1 [-1.6, -0.7]	<0.001	-0.2 [-0.8, 0.4]	0.561
Perceived availability of support – emotional		-0.8 [-1.3, -0.4]	<0.001	-0.9 [-1.3, -0.4]	<0.001	-0.04 [-0.6, 0.5]	0.900
HIV-related stigma – social rejection		2.2 [1.7, 2.7]	<0.001	2.2 [1.7, 2.7]	<0.001	0.7 [0.1, 1.3]	0.025
HIV-related stigma – internalised shame		2.2 [1.8, 2.6]	<0.001	2.2 [1.8, 2.6]	<0.001	1.8 [1.2, 2.3]	<0.001

[1] Regression coefficient [95% CI] adjusted for age, marital status and pregnancy intention; [3] Regression coefficient [95% CI] adjusted for all other covariates in model

Figure 4.1.1 Mean (SD) depression score across tertiles of HIV-related stigma, stratified by tertiles of social support

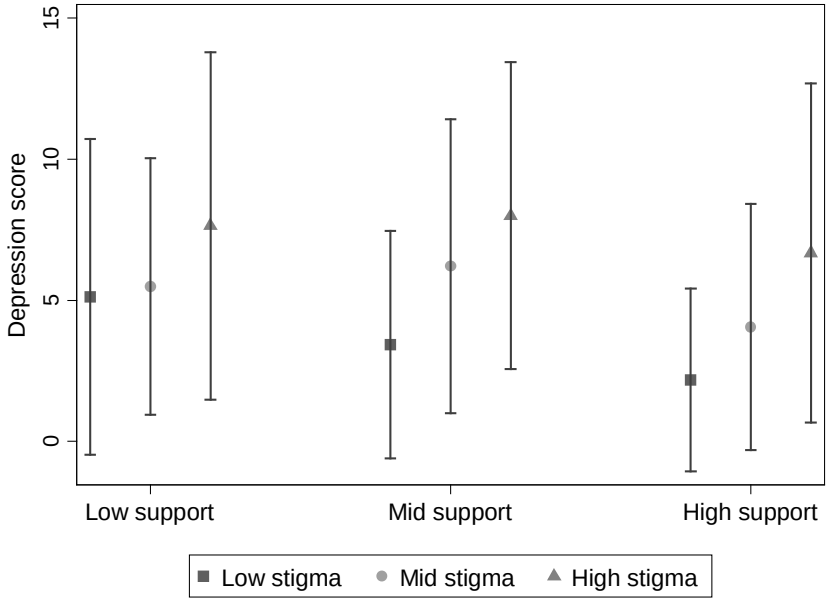
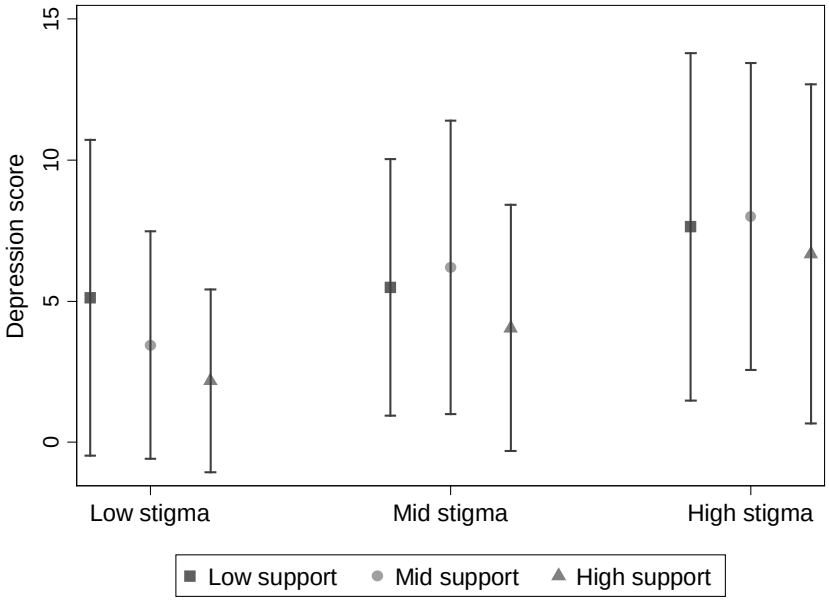


Figure 4.1.2 Mean (SD) depression score across tertiles of social support, stratified by tertiles of HIV-related stigma



4.4 Discussion

This research explored variables associated with the perceived availability of social support and HIV-related stigma in a sample of HIV-infected pregnant women in South Africa, and examined the interrelationships among these factors and antenatal depressive symptoms. Social support and HIV-related stigma were observed to be highly interrelated in this sample, with strong and persistent associations observed between these constructs, and between poverty and decreased levels of instrumental support. A high proportion of participants scored above suggested thresholds on the EPDS, with one in five women scoring ≥10, and one in ten scoring ≥13. Social rejection and internalised shame were found to be strongly associated with depression scores in this sample, with stronger effects observed for internalised shame. Although associations were observed between social support and depression scores in unadjusted analyses, stigma was observed to moderate this association, with social support only associated with depression scores when low levels of stigma were reported. In contrast, an association between stigma and depression scores was observed at all levels of social support, suggesting that social support does not act as a buffer against the detrimental effects of stigma in this sample.

Although slightly lower than other recently reported estimates among pregnant women in the region [29-31], the proportion of participants with elevated depression scores observed here is concerning, given documented adverse effects on maternal and child health and on HIV-related treatment outcomes. Although much progress has been made in improving maternal physical health, this persistently high prevalence of depressive symptoms suggests that more focus is needed on mental health in this population. The variables associated with depression scores observed here are well-documented risk factors for depression during pregnancy, although here they are described among a population of women among whom a dearth of

data exist. As this population grows, understanding and targeting these barriers to optimal mental health will become increasingly important to ensure long-term maternal and child health.

The finding that stigma moderates the relationship between social support and depression scores is notable, and contrasts with previous research conducted among HIV-infected men and women in the Western Cape, South Africa, where both social support and stigma were found to be independently associated with depression [18]. This novel finding highlights the urgent need for interventions to reduce stigma in this context, particularly given its adverse effects in HIV-infected pregnant women who may already be at increased risk of depression. While much progress has been made in the stigma-reduction field, many gaps and challenges remain in developing effective interventions and incorporating them into national HIV programmes [32], and the need for evidence-based interventions has been widely described. Our findings highlight the need for an increased focus on preventive interventions to reduce stigma, particularly given the well-documented adverse effects of antenatal depression and the relative lack of effective treatment resources in LMICs [4, 6]. Although many interventions to increase social support for HIV-infected individuals have been posited, our findings suggest that increasing social support may not be sufficient in contexts where stigma is prevalent, and community- and structural-level approaches to alleviate stigma, which are currently rare [33], are urgently needed.

In this low socioeconomic context, higher levels of poverty were identified as a risk factor for both higher levels of HIV-related stigma and lower levels of social support, and the relationship between poverty and instrumental support persisted in adjusted analyses. For women in adverse socioeconomic circumstances, instrumental support may be lacking if

friends and family are similarly living in poverty. Alternatively, women may require additional support to request assistance from friends and family, especially in contexts where stigma is prevalent. Interestingly, the perceived availability of instrumental support had stronger effects on depression scores in unadjusted analyses than did the perceived availability of emotional support. This is consistent with the findings of previous research in KwaZulu-Natal, South Africa [24], and may indicate that structural interventions to alleviate poverty may have a greater impact than interventions to increase emotional social support in these contexts. These interventions may be particularly beneficial among pregnant women, where financial constraints may be compounded by factors such as transport costs when accessing antenatal care, as well as increased household expenses after delivery.

A particular strength of this study is the inclusion of a large sample recruited from a primary care clinic, as the results observed are likely to be generalisable to other communities in the region. In addition, the inclusion of multiple psychological constructs in one analysis and the exploration of the complex interrelationships between them is a novel aspect of the present study, given the dearth of similar data in this context. A limitation of the present analysis, however, is that all of the data included were based on self-report and may be subject to social desirability bias. Although the EPDS has been validated for use as a screening tool in a South African population [28], the use of self-reported depressive symptoms may not reflect the true prevalence of antenatal depression in this population. Since this measure is not a diagnostic assessment, it may additionally be picking up on generalised psychiatric distress, including symptoms of anxiety, even though it was developed specifically as a measure of depression. As this study was a cross-sectional analysis of baseline data, we cannot make inferences regarding causality among these variables. Recent research has demonstrated a dynamic relationship between social support and stigma [33], a finding which warrants

further exploration using other longitudinal datasets. In addition, it is possible that depression causes increases in reported stigma as well as decreases in the perceived availability of social support, a hypothesis that we were unable to explore in these cross-sectional data and that has major implications for the development of interventions in this context.

Despite these limitations, the findings from the present study are notable, and add to the literature in several important ways. Few data examining psychosocial risk factors among women initiating ART in the context of Option B+ exist, and the present study is notable in that it explores these constructs in this important population. As increasing numbers of women initiate ART during pregnancy, understanding the psychosocial risk factors faced by these women will become increasingly important, given their possible impact on adherence and retention in care. The present analysis is notable in that it begins to explore these constructs, and highlights the importance of simultaneously considering the associations among multiple psychosocial risk factors and depressive symptoms in order to generate a more nuanced understanding of the complex interrelationships among these constructs. In particular, this analysis highlights the moderating role of HIV-related stigma in the relationship between social support and depressive symptoms in this population. These results suggest that research to identify ways of reducing stigma and increased efforts to alleviate stigma, particularly at the community and structural level, are urgently needed. Finally, these findings suggest that further study of the impact of psychosocial factors on HIV-related outcomes, including ART adherence and retention in care, is needed in this population.

References

1. Walker SP, Wachs TD, Meeks Gardner J, Lozoff B, Wasserman GA, Pollitt E, et al. Child development: risk factors for adverse outcomes in developing countries. The Lancet. 2007;369(9556):145-157.
2. Walker SP, Wachs TD, Grantham-McGregor S, Black MM, Nelson CA, Huffman SL, et al. Inequality in early childhood: risk and protective factors for early child development. The Lancet. 2011;378(9799):1325-1338.
3. World Health Organization, United Nations Population Fund. Mental health aspects of women's reproductive health: a global review of the literature. Geneva: World Health Organization; 2009.
4. Stein A, Pearson RM, Goodman SH, Rapa E, Rahman A, McCallum M, et al. Effects of perinatal mental disorders on the fetus and child. The Lancet. 2014;384(9956):1800-1819.
5. Brittain K, Myer L, Koen N, Koopowitz S, Donald KA, Barnett W, et al. Risk factors for antenatal depression and associations with infant birth outcomes: results from a South African birth cohort study. Paediatr Perinat Epidemiol. 2015;29(6):505-514.
6. Howard LM, Molyneaux E, Dennis C-L, Rochat T, Stein A, Milgrom J. Non-psychotic mental disorders in the perinatal period. The Lancet. 2014;384(9956):1775-1788.
7. Kapetanovic S, Dass-Brailsford P, Nora D, Talisman N. Mental health of HIV-seropositive women during pregnancy and postpartum period: a comprehensive literature review. AIDS Behav. 2014;18(6):1152-1173.
8. Kotzé M, Visser M, Makin J, Sikkema K, Forsyth B. Psychosocial variables associated with coping of HIV-positive women diagnosed during pregnancy. AIDS Behav. 2013;17(2):498-507.
9. Peltzer K, Ramlagan S. Perceived stigma among patients receiving antiretroviral therapy: a prospective study in KwaZulu-Natal, South Africa. AIDS Care. 2011;23(1):60-68.
10. Nel A, Kagee A. Common mental health problems and antiretroviral therapy adherence. AIDS Care. 2011;23(11):1360-1365.
11. Krumme AA, Kaigamba F, Binagwaho A, Murray MB, Rich ML, Franke MF. Depression, adherence and attrition from care in HIV-infected adults receiving antiretroviral therapy. J Epidemiol Community Health. 2015;69(3):284-289.
12. O'Hiarlaithe M, Grede N, de Pee S, Bloem M. Economic and social factors are some of the most common barriers preventing women from accessing maternal and newborn child health (MNCH) and prevention of mother-to-child transmission (PMTCT) services: a literature review. AIDS Behav. 2014;18:S516-S530.
13. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. J Int AIDS Soc. 2013;16:18588.
14. Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J, et al. A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women PLoS ONE. 2014;9(11):e111421.

15. Seth P, Kidder D, Pals S, Parent J, Mbatia R, Chesang K, et al. Psychosocial functioning and depressive symptoms among HIV-positive persons receiving care and treatment in Kenya, Namibia, and Tanzania. Prev Sci. 2014;15:318-328.
16. Endeshaw M, Walson J, Rawlins S, Dessie A, Alemu S, Andrews N, et al. Stigma in Ethiopia: association with depressive symptoms in people with HIV. AIDS Care. 2014;26(8):935-939.
17. Onyebuchi-Iwudibia O, Brown A. HIV and depression in eastern Nigeria: the role of HIV-related stigma. AIDS Care. 2014;26(5):653-657.
18. Breet E, Kagee A, Seedat S. HIV-related stigma and symptoms of post-traumatic stress disorder and depression in HIV-infected individuals: does social support play a mediating or moderating role? AIDS Care. 2014;26(8):947-951.
19. World Health Organization. Programmatic update: use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. Geneva: World Health Organization; 2012 [accessed 2015, Sep 21]. Available from: http://www.who.int.hiv/PMTCT_update.pdf
20. Kaplan R, Orrell C, Lawn SD, Bekker L-G, Wood R. The Hannan Crusaid treatment centre - early beginnings and lessons learnt. S Afr J HIV Med. 2014;15(1):35-37.
21. Strategic Development Information, City of Cape Town GIS Department. City of Cape Town - Census 2011 – Gugulethu. 2011 [accessed 2015, Sep 8]. Available from: http://www.capetown.gov.za/en/stats/2011CensusSuburbs/2011_Census_CT_Suburb_Gugulethu_Profile.pdf
22. Barrera MA. A method for assessing social support networks in community survey research. Connections. 1980;3(3):8-13.
23. Arnsten JH, Li X, Mizuno Y, Knowlton AR, Gourevitch MN, Handley K, et al. Factors associated with antiretroviral therapy adherence and medication errors among HIV-infected injection drug users. J Acquir Immune Defic Syndr. 2007;46:S64-S71.
24. Yeji F, Klipstein-Grobusch K, Newell M-L, Hirschhorn LR, Hosegood V, Bärnighausen T. Are social support and HIV coping strategies associated with lower depression in adults on antiretroviral treatment? Evidence from rural KwaZulu-Natal, South Africa. AIDS Care. 2014;26(12):1482-1489.
25. Fife BL, Wright ER. The dimensionality of stigma: a comparison of its impact on the self of persons with HIV/AIDS and cancer. J Health Soc Behav. 2000;41(1):50-67.
26. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987;150:782-786.
27. Murray D, Cox JL. Screening for depression during pregnancy with the Edinburgh Depression Scale (EDDS). J Reprod Infant Psychol. 1990;8(2):99-107.
28. Lawrie TA, Hofmeyr GJ, de Jager M, Berk M. Validation of the Edinburgh Postnatal Depression Scale on a cohort of South African women. S Afr Med J. 1998;88(10):1340-1344.
29. Tsai AC, Tomlinson M, Dewing S, le Roux IM, Harwood JM, Chopra M, et al. Antenatal depression case finding by community health workers in South Africa: feasibility of a mobile phone application. Arch Womens Ment Health. 2014;17:423-431.
30. Baron E, Field S, Kafaar Z, Honikman S. Patterns of use of a maternal mental health service in a low-resource antenatal setting in South Africa. Health Soc Care Community. 2015;23(5):502-512.

31. Schneider M, Baron E, Davies T, Bass J, Lund C. Making assessment locally relevant: measuring functioning for maternal depression in Khayelitsha, Cape Town. Soc Psychiatry Psychiatr Epidemiol. 2015;50:797-806.
32. Stangl A, Lloyd JK, Brady LM, Holland CE, Baral S. A systematic review of interventions to reduce HIV-related stigma and discrimination from 2002 to 2013: how far have we come? J Int AIDS Soc. 2013;16(3 Suppl 2):18734.
33. Takada S, Weiser SD, Kumbakumba E, Muzoora C, Martin JN, Hunt PW, et al. The dynamic relationship between social support and HIV-related stigma in rural Uganda. Ann Behav Med. 2014;48:26-37.

Chapter 5: HIV-status disclosure and depression in the context of unintended pregnancy among South African women

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Author contributions

KB conceptualised and conducted the analysis, led data interpretation and drafted the manuscript. TP and AZ directed data collection and assisted with data interpretation. EJA and LM conceptualised the study from which these data arise, were responsible for funding, implementation and overall leadership, and assisted with data interpretation. CAM and RHR contributed to study design and assisted with data interpretation. All authors read and approved the final manuscript.

Abstract

Depressive symptoms are common among pregnant women living with HIV, and an unintended pregnancy may heighten vulnerability. HIV-status disclosure is thought to improve psychological well-being, but few quantitative studies have explored the relationships among disclosure, pregnancy intention and depression. Using multivariable linear regression models, we examined the impact of disclosure on depressive symptoms (Edinburgh Postnatal Depression Scale; EPDS) during pregnancy and postpartum among women who tested HIV-positive during the pregnancy in South Africa; and explored the role of pregnancy intention in this relationship. Among 350 women (median age: 27 years; 70% reporting that their current pregnancy was unintended), neither disclosure to a male partner nor disclosure to ≥1 family/community member had a consistent effect on depressive symptoms. However, pregnancy intention modified the association between disclosure to a male partner and depression during pregnancy: disclosure was associated with higher depression scores among women who reported that their current pregnancy was unintended but was associated with lower depression scores among women who reported that their pregnancy was intended. During the early postpartum period, disclosure to ≥1 family/community member was associated with higher depression scores. Counselling around disclosure in pregnancy should consider the heightened vulnerability that women face when experiencing an unintended pregnancy.

5.1 Introduction

Pregnant women living with HIV experience high rates of depressive symptoms globally [1]. In general populations of pregnant women, antenatal depression has well-documented negative effects on maternal health [2] and child health and development [3]; in the context of HIV, depression may have additional negative effects on the uptake of prevention of mother-to-child HIV transmission services [4, 5]. In South Africa, women undergo routine HIV testing when entering antenatal care, and a new HIV diagnosis during pregnancy may lead to heightened vulnerability. In this context, women face a 'triple burden' of transitioning into pregnancy, accepting their HIV diagnosis, and accepting the urgent need to start lifelong antiretroviral therapy (ART) [6]. This vulnerability may be further heightened by an unintended pregnancy. Unintended pregnancies are common among women living with HIV in South Africa [7, 8] and may lead to considerable disruption in women's lives [9] as well as antenatal depression [10-12].

Self-disclosure of HIV status to others within an individual's social network is widely encouraged in counselling services for people living with HIV, and is thought to have beneficial effects on psychological well-being. However, the evidence for this association is mixed [13]. Among adults living with HIV, cross-sectional studies have reported that disclosure is associated with either higher [14, 15] or lower [16, 17] levels of depression; other studies have found no association [18-20]. In longitudinal studies, depression appears to be associated with lower levels of disclosure to sexual partners among men who have sex with men [21] as well as among women living with HIV [22], with higher levels of depression associated with a longer time to first disclosure among women living with HIV in the United States [23]. It has been suggested that the association between disclosure and lower levels of depression is mediated by social support [17], with disclosure being beneficial

only to the extent to which it alleviates psychological stress or provides a mechanism to obtain social support [13]. In contrast, negative responses to disclosure may be associated with lower levels of perceived social support and higher levels of psychological distress [24].

Qualitative work among pregnant and postpartum women living with HIV in Uganda has documented an evolution of coming to terms with an HIV diagnosis and developing coping strategies, with disclosing and receiving support described as integral to this process [25]. However, few quantitative studies have examined the role of pregnancy intention in the relationship between disclosure and psychological well-being among pregnant women living with HIV. In the context of an unintended pregnancy and an HIV diagnosis during pregnancy, women must negotiate a dual disclosure: disclosure of the unintended pregnancy as well as disclosure of their HIV status [9]. Given the well-documented negative effects of antenatal depression among pregnant women living with HIV, and heightened vulnerability due to an unintended pregnancy, studies are needed to examine the relationships among disclosure, pregnancy intention and depression. We thus examined the impact of HIV-status disclosure on depression during pregnancy and postpartum among women who tested HIV-positive during the pregnancy; and explored the role of the intendedness of the current pregnancy in this relationship.

5.2 Materials and methods

5.2.1 Study design

These analyses use data from a multi-phase implementation science study, the MCH-ART study, which evaluated strategies for delivering HIV care and treatment services during pregnancy and the postpartum period in Cape Town, South Africa (ClinicalTrials.gov NCT01933477). The design and primary results of the study have been previously described

[26, 27]. Briefly, the study was conducted at one antenatal care clinic in the former township of Gugulethu, where an antenatal HIV prevalence of ~30% has been documented [28]. The study included a cross-sectional evaluation of all pregnant women living with HIV who were entering antenatal care; an observational cohort following women who initiated ART during the pregnancy through their first postpartum clinic visit; and an intervention study evaluating strategies for delivering HIV care and treatment services to breastfeeding women through 12 months postpartum. ART eligibility was determined based on local guidelines in this setting: until June 2013, eligibility was determined based on CD4 cell count or clinical disease staging; from July 2013 onward, all pregnant women living with HIV were eligible to initiate lifelong ART under the World Health Organization's Option B+ guidelines [29].

5.2.2 Participants

For the broader MCH-ART study, women who initiated ART during the pregnancy were followed through delivery, and women opting to breastfeed were followed through 12 months postpartum. For the current analyses, we included women who had tested HIV-positive during the pregnancy and who were initiating ART in analyses through 12 months postpartum. Participants were enrolled into the study between March 2013 and April 2014. All women provided written informed consent prior to enrolment, and the study was approved by the University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee and by Columbia University Medical Center's Institutional Review Board in New York.

5.2.3 Measures

Participants attended study measurement visits that were separate from routine HIV or antenatal/postpartum care. Study measures were administered by trained interviewers in isiXhosa, the predominant local language. Measures were translated from English into isiXhosa and were back-translated prior to the study using standard procedures to ensure accuracy [30]. Basic sociodemographic characteristics were assessed at enrolment into the study, which coincided with participants' entry into antenatal care, and included age, educational attainment and relationship status. The intendedness of the current pregnancy was assessed by asking women whether or not they were trying to have a baby when they found out that they were pregnant. A composite poverty score was calculated in order to categorise participants according to relative levels of disadvantage, and was based on current employment, housing type and access to household assets [31]. At entry into antenatal care, women underwent phlebotomy for CD4 enumeration via flow cytometry (Beckman Coulter), and gestation was assessed using ultrasound.

HIV-status disclosure was self-reported at all study visits using a tool previously described [32]. Briefly, disclosure was assessed by asking women whether they had told their male partner about their HIV status, as well as whether they had told family/community members, including their mother, father, sister, brother, uncle, aunt, male cousin, female cousin, other male family member, other female family member, friend, or spiritual leader. This list of individuals was developed for the purposes of this study, and disclosure to each category was assessed using response options of 'Yes', 'No', or 'Not Applicable'; we combined the response options 'No' and 'Not applicable' in analyses.

Self-reported depressive symptoms were assessed at three timepoints (participants' 2nd antenatal visit and at 6 weeks and 12 months postpartum) using the 10-item Edinburgh Postnatal Depression Scale (EPDS) [33]. The EPDS was originally developed as a screening tool for possible depressive disorders among postpartum women, but has been validated for use in pregnancy [34] and in a sample of postpartum women in South Africa [35]. Based on the original development of the scale, each item was assessed on a frequency scale ranging from 0 to 3, and a total score was obtained by summing individual item responses, with higher scores indicating more severe depressive symptoms. We used a threshold value of ≥13 as suggestive of elevated depressive symptoms in descriptive analyses, as recommended in the original development of the scale [33].

5.2.4 Data analysis

Data were analysed using Stata 14 (StataCorp Inc, College Station, Texas, USA). Baseline sociodemographic characteristics were summarised and were compared across pregnancy intention using Wilcoxon rank sum (Mann-Whitney) tests for non-normally distributed continuous variables, and chi-square and Fisher's exact tests for categorical variables. For each timepoint at which depressive symptoms were assessed, we used multivariable linear regression models to explore the associations between cumulative reports of disclosure up to that study visit and depressive symptoms, adjusting for potential confounding by sociodemographic characteristics and, at postpartum timepoints, design effect. We explored the impact of the intendedness of the current pregnancy in stratified models and using interaction terms. Throughout, we explored disclosure using two separate constructs: (i) disclosure to a male partner and (ii) disclosure to ≥1 family/community member, based on previous analyses suggesting that these disclosure events form separate dimensions in this sample [32]. Continuous depressive symptom scores were used in all analyses, although the

proportion of participants with elevated scores on the EPDS was calculated at each timepoint using the suggested threshold value described above. Finally, we repeated our analysis restricted to women who had completed assessments at all three timepoints in order to assess potential changes in results (*n*=208). This restriction did not change results, thus we present results from the total sample below.

5.3 Results

5.3.1 Participant characteristics, disclosure and depressive symptoms

A total of 350 women (median age: 26.9 years) who had tested HIV-positive during the pregnancy, were eligible to initiate ART, and completed assessments at the 2nd antenatal study visit were included in analyses. A total of 258 women (74%) completed assessments at the 6 week postpartum study visit, and 213 (61%) completed assessments at 12 months postpartum. Sociodemographic and clinical characteristics are presented in Table 5.1, stratified by pregnancy intention. Most participants reported a previous pregnancy, and reported low levels of educational attainment and employment; 70% of women reported that their current pregnancy was unintended. Women who reported an unintended pregnancy were significantly less likely to be married and/or cohabiting with their partner ($p<0.001$) and had entered antenatal care at a significantly later gestation ($p=0.006$).

Table 5.1 Participant characteristics, HIV-status disclosure and depressive symptoms (Edinburgh Postnatal Depression Scale; EPDS), by intendedness of the current pregnancy

		Pregnancy intention		
Variable	Total sample – *n* (%)	Unintended – *n* (%)	Intended – *n* (%)	*P*-value
Number of women	350	244	106	
Participant sociodemographic and clinical characteristics at entry into antenatal care				
Median [IQR] age in years	26.9 [23.5, 31.5]	26.7 [23.1, 31.4]	27.5 [24.3, 31.6]	0.268
Educational attainment				
Primary/some secondary	241 (69)	167 (68)	74 (70)	
Completed secondary/any tertiary	109 (31)	77 (32)	32 (30)	0.799
Currently employed	146 (42)	103 (42)	43 (41)	0.774
Poverty level (assets + employment)				
Most disadvantaged	123 (35)	88 (36)	35 (33)	
Moderately disadvantaged	116 (33)	80 (33)	36 (34)	
Least disadvantaged	111 (32)	76 (31)	35 (33)	0.857
Married and/or cohabiting	130 (37)	72 (30)	58 (55)	<0.001
First pregnancy	95 (27)	65 (27)	30 (28)	0.748
Median [IQR] gestation in weeks	21 [16, 26]	22 [17, 28]	20 [15, 24]	0.006
Median [IQR] CD4 cell count (*n*=337)	352 [247, 504]	352 [248, 513]	351 [247, 504]	0.602
HIV-status disclosure				
Disclosed to male partner by 2nd antenatal visit	188 (54)	120 (49)	68 (64)	0.010
Disclosed to male partner by 6 weeks postpartum (*n*=258)	150 (58)	101 (54)	49 (68)	0.045
Disclosed to male partner by 12 months postpartum (*n*=213)	127 (60)	85 (57)	42 (67)	0.175
Disclosed to ≥1 family/community member by 2nd antenatal visit	202 (58)	141 (58)	61 (58)	0.967
Disclosed to ≥1 family/community member by 6 weeks postpartum (*n*=258)	169 (66)	119 (64)	50 (69)	0.407
Disclosed to ≥1 family/community member by 12 months postpartum (*n*=213)	155 (73)	107 (71)	48 (76)	0.467
Depressive symptoms				
EPDS score ≥13 at 2nd antenatal visit	41 (12)	30 (12)	11 (10)	0.608
EPDS score ≥13 at 6 weeks postpartum (*n*=258)	11 (4)	8 (4)	3 (4)	0.962
EPDS score ≥13 at 12 months postpartum (*n*=213)	10 (5)	7 (5)	3 (5)	0.976

Reported disclosure to a male partner increased from 54% of participants at the 2nd antenatal study visit to 60% at 12 months postpartum; disclosure to ≥1 family/community member increased from 58% to 73% (Table 5.1). Few sociodemographic or clinical characteristics were associated with disclosure, but women who were married and/or cohabiting were more likely to report having disclosed to their male partner and less likely to report having disclosed to ≥1 family/community member (both $p<0.001$) at the 2nd antenatal study visit. Women who reported that their current pregnancy was intended were also more likely to report having disclosed to a male partner by their 2nd antenatal study visit compared to women who reported that their current pregnancy was unintended ($p=0.010$). The proportion of women scoring above threshold for depressive symptoms decreased from 12% at the 2nd antenatal study visit, to 4% and 5% at the 6 week and 12 month postpartum study visits, respectively; levels of depressive symptoms were similar when restricted to women with complete data across all three timepoints. No differences in depressive symptoms were observed across the intendedness of the current pregnancy.

5.3.2 Impact of disclosure on antenatal depressive symptoms

Overall, neither disclosure to a male partner nor disclosure to ≥1 family/community member was associated with depressive symptoms at the 2nd antenatal study visit (Table 5.2), with results unchanged when stratified by relationship status and by age categories. However, pregnancy intention appeared to modify the association between disclosure to a male partner and depressive symptoms. Among women who reported that their current pregnancy was unintended, disclosure to a male partner was associated with *higher* depression scores in both unadjusted models [regression coefficient (β): 1.53; 95% confidence interval (CI): 0.17, 2.89] and after adjustment for sociodemographic characteristics (β: 1.59; 95% CI: 0.21, 2.97). Conversely, disclosure to a male partner was associated with *lower* depression scores among

women who reported that their current pregnancy was intended after adjusting for sociodemographic characteristics (β: -2.27; 95% CI: -4.48, -0.07). Effect modification by pregnancy intention was clearly observed in a graphical portrayal of mean depressive symptom scores: on average, depressive symptom scores were highest among women who reported that the current pregnancy was unplanned and disclosed to their male partner, and among women who reported that the current pregnancy was planned but did not disclose to their male partner (Figure 5.1.1). Stratification by pregnancy intention did not change the null association between disclosure to ≥1 family/community member and depressive symptoms.

5.3.3 Impact of disclosure on postpartum depressive symptoms

At 6 weeks postpartum, no associations were observed between disclosure to a male partner and depressive symptoms in unadjusted models or after adjustment for age, poverty, relationship status and design effect; these null results persisted when stratified by pregnancy intention. However, disclosure to ≥1 family/community member was associated with *higher* depression scores at this timepoint (β: 1.10; 95% CI: 0.07, 2.12 in unadjusted model; and β: 0.94; 95% CI: -0.11, 1.99 after adjustment for age, poverty, relationship status and design effect); this association was stronger among women who reported that the current pregnancy was intended (β: 1.92; 95% CI: 0.10, 3.74 in unadjusted model; and β: 1.94; 95% CI: -0.03, 3.91 after adjustment for age, poverty, relationship status and design effect; Figure 5.1.2). In the total sample at 12 months postpartum, neither disclosure to a male partner nor disclosure to ≥1 family/community member was associated with depressive symptoms in unadjusted models or after adjustment for age, poverty, relationship status and design effect; these null results persisted when stratified by pregnancy intention (Figure 5.1.3).

Table 5.2 Impact of disclosure on depressive symptoms at 2nd antenatal visit, overall and by intendedness of the current pregnancy (*n*=350)

Variable	Mean (SD) EPDS score[1]	Unadjusted β [95% CI][2]	*P*-value	Adjusted β [95% CI][3]	*P*-value
All women					
Disclosure to a male partner					
Has not disclosed	5.1 (5.3)	Reference		Reference	
Has disclosed	5.5 (5.3)	0.44 [-0.68, 1.56]	0.443	0.51 [-0.65, 1.67]	0.388
Disclosure to family/community members					
Disclosed to none	5.1 (5.3)	Reference		Reference	
Disclosed to ≥1 person	5.5 (5.3)	0.45 [-0.68, 1.58]	0.435	0.45 [-0.70, 1.60]	0.443
Women reporting unintended pregnancy at 1st antenatal visit					
Disclosure to a male partner					
Has not disclosed	4.8 (5.2)	Reference		Reference	
Has disclosed	6.3 (5.6)	1.53 [0.17, 2.89]	0.027	1.59 [0.21, 2.97]	0.025
Disclosure to family/community members					
Disclosed to none	5.3 (5.4)	Reference		Reference	
Disclosed to ≥1 person	5.7 (5.5)	0.44 [-0.95, 1.83]	0.532	0.53 [-0.89, 1.94]	0.463
Women reporting intended pregnancy at 1st antenatal visit					
Disclosure to a male partner					
Has not disclosed	6.1 (5.5)	Reference		Reference	
Has disclosed	4.2 (4.6)	-1.97 [-3.96, 0.03]	0.053	-2.27 [-4.48, -0.07]	0.043
Disclosure to family/community members					
Disclosed to none	4.6 (5.0)	Reference		Reference	
Disclosed to ≥1 person	5.1 (5.1)	0.47 [-1.50, 2.43]	0.640	0.25 [-1.81, 2.30]	0.813

[1] SD: standard deviation; EPDS: Edinburgh Postnatal Depression Scale; [2] β: regression coefficient; [3] adjusted for age, poverty and relationship status

Figure 5.1.1 Mean (SD) depressive symptom scores at the 2nd antenatal study visit by disclosure to a male partner and to ≥1 family/community member, stratified by intendedness of the current pregnancy

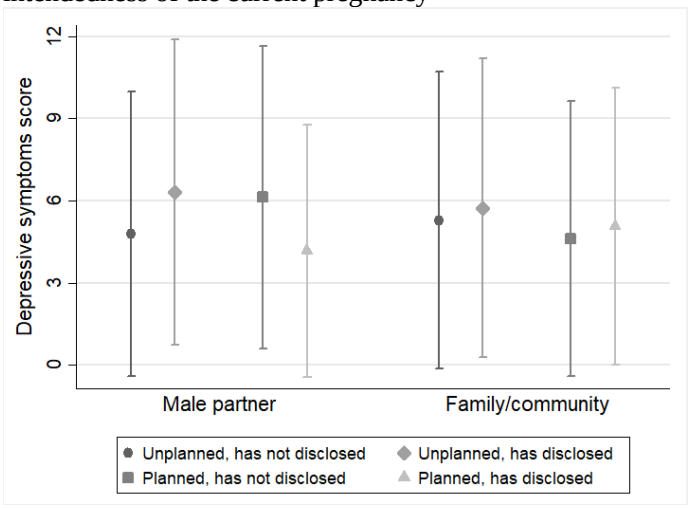
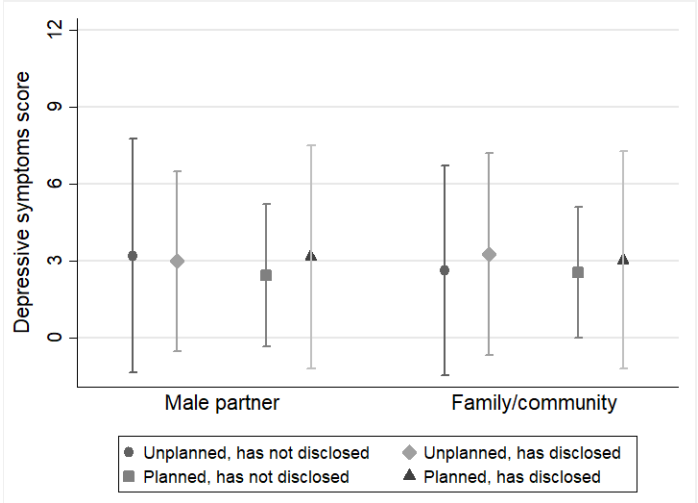


Figure 5.1.2 Mean (SD) depressive symptom scores at the 6 week postpartum study visit by disclosure to a male partner and to ≥1 family/community member, stratified by intendedness of the current pregnancy

Figure 5.1.3 Mean (SD) depressive symptom scores at the 12 month postpartum study visit by disclosure to a male partner and to ≥1 family/community member, stratified by intendedness of the current pregnancy



5.4 Discussion

This research examined the impact of HIV-status disclosure on depression during pregnancy and postpartum among women who had tested HIV-positive during the pregnancy; and explored the role of the intendedness of the current pregnancy in this relationship. The proportion of women with elevated depressive symptoms was high antenatally, but decreased during the postpartum period. Both unintended pregnancy and disclosure were common, and neither disclosure to a male partner nor disclosure to ≥1 family/community member was consistently associated with antenatal or postpartum depressive symptoms in the overall sample. However, the association between disclosure to a male partner and antenatal depressive symptoms was modified by the intendedness of the current pregnancy: disclosure was associated with higher depression scores among women who reported that their current pregnancy was unintended, but was associated with lower depression scores among women who reported that their current pregnancy was intended. During the early postpartum period, disclosure to ≥1 family/community member was associated with higher depression scores, but this association did not persist at 12 months postpartum.

Several key findings warrant further discussion. First, women receiving a new HIV diagnosis in the context of an unintended pregnancy face additional vulnerability. Fears about disclosing are common among women living with HIV, with women fearing abandonment and intimate partner violence after disclosing to a partner, and gossip and discrimination after disclosing to community members [36]. In the context of an unintended pregnancy as well as a new HIV diagnosis, the dual disclosure that women must negotiate has been described as a 'double disclosure bind' [9]. We have previously shown that disclosure to a male partner during pregnancy and postpartum is more common among women reporting an intended pregnancy [32]. Here, we have demonstrated that the intendedness of the pregnancy

additionally modifies the impact of disclosure to a male partner on depressive symptoms. In the context of an unintended pregnancy, women who disclosed their HIV status to their male partner reported higher levels of depressive symptoms during pregnancy compared to women who did not disclose. This effect did not persist during the postpartum period, and we hypothesise that this may indicate an evolution of coming to terms both with a new HIV diagnosis and with an unintended pregnancy. Further research is needed to explore this possibility, and to explore the causality of our findings.

Second, these results highlight the importance of considering women's relationships with the person(s) to whom they disclose. Most existing research operationalises disclosure as any versus no disclosure [37], or focusses only on disclosure to a partner. Our findings suggest that disclosure to different individuals may have different effects on depression; previous research has similarly shown that the impact of disclosure depends on women's relationships with the person(s) to whom they have disclosed [38]. Further, our findings may explain the mixed evidence in the existing literature, where studies have mostly used simplified measures of disclosure as well as cross-sectional analyses. Finally, we observed a reduction in the proportion of women with elevated depressive symptoms in the postpartum compared to antenatal period, similar to findings from Malawi [39]. We included only women who had been diagnosed HIV-positive during the pregnancy in analyses, and thus hypothesise that a new HIV diagnosis may have led to a high prevalence of antenatal depressive symptoms, but that this prevalence decreased during the postpartum period as women came to terms with their diagnosis. Further research is needed to explore the evolution of depressive symptoms over time in this population.

A strength of the present study is the inclusion of longitudinal data as well as the use of disclosure measures that allowed for the consideration of women's relationships to the person(s) to whom they had disclosed. In addition, we included a large sample of women who tested HIV-positive at a primary care facility, and our findings are likely to be generalisable to other communities of pregnant and postpartum women in the region. A limitation of this analysis is the use of self-report to measure disclosure. In addition, depressive symptoms were assessed using self-report and not a diagnostic interview. Self-reported disclosure may be subject to recall and social desirability bias, although this is common to all disclosure research, and the EPDS has been validated in pregnancy and in postpartum women in South Africa. A further limitation of this analysis is that we did not assess responses to disclosure, which may be critical determinants of subsequent psychological well-being or distress. Finally, we did not examine associations between disclosure and other psychosocial variables, and our findings should be extrapolated to other markers of psychological well-being with caution.

Despite some limitations, these results are novel and the findings notable. There is limited quantitative evidence for a beneficial effect of disclosure on depression among pregnant women living with HIV, and a dearth of research examining the role of the intendedness of the pregnancy in this relationship. Our findings suggest that disclosure does not have a consistent effect on depression; rather, disclosure to a male partner appears to have an adverse effect during the antenatal period among women experiencing an unintended pregnancy, and a beneficial effect among women experiencing an intended pregnancy. Although these findings did not persist during the postpartum period, we argue that they have important implications for counselling services during pregnancy, given the well-documented adverse effects of antenatal depression. Without consideration of pregnancy intention, as well

as women's relationships to the person(s) to whom they disclose, counselling services may be encouraging women to disclose when this may have negative repercussions. Our findings suggest that counselling messaging around HIV-status disclosure in pregnancy should consider the heightened vulnerability that women face when experiencing an unintended pregnancy, and that disclosure may not be beneficial for all women.

References

1. Kapetanovic S, Dass-Brailsford P, Nora D, Talisman N. Mental health of HIV-seropositive women during pregnancy and postpartum period: a comprehensive literature review. AIDS Behav. 2014;18(6):1152-1173.
2. World Health Organization, United Nations Population Fund. Mental health aspects of women's reproductive health: a global review of the literature. Geneva: World Health Organization; 2009.
3. Stein A, Pearson RM, Goodman SH, Rapa E, Rahman A, McCallum M, et al. Effects of perinatal mental disorders on the fetus and child. The Lancet. 2014;384(9956):1800-1819.
4. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. J Int AIDS Soc. 2013;16:18588.
5. O'Hiarlaithe M, Grede N, de Pee S, Bloem M. Economic and social factors are some of the most common barriers preventing women from accessing maternal and newborn child health (MNCH) and prevention of mother-to-child transmission (PMTCT) services: a literature review. AIDS Behav. 2014;18:S516-S530.
6. Stinson K, Myer L. Barriers to initiating antiretroviral therapy during pregnancy: a qualitative study of women attending services in Cape Town, South Africa. Afr J AIDS Res. 2012;11(1):65-73.
7. Adeniyi OV, Ajayi AI, Moyaki MG, Goon DT, Avramovic G, Lambert J. High rate of unplanned pregnancy in the context of integrated family planning and HIV care services in South Africa. BMC Health Serv Res. 2018;18(1):140.
8. Iyun V, Brittain K, Phillips TK, le Roux S, Mcintyre JA, Zerbe A, et al. Prevalence and determinants of unplanned pregnancy in HIV-positive and HIV-negative pregnant women in Cape Town, South Africa: a cross-sectional study. BMJ Open. 2018;8:e019979.
9. Crankshaw TL, Voce A, King RL, Giddy J, Sheon NM, Butler LM. Double disclosure bind: complexities of communicating an HIV diagnosis in the context of unintended pregnancy in Durban, South Africa. AIDS Behav. 2014;18:S53-S59.
10. Brittain K, Myer L, Koen N, Koopowitz S, Donald KA, Barnett W, et al. Risk factors for antenatal depression and associations with infant birth outcomes: results from a South African birth cohort study. Paediatr Perinat Epidemiol. 2015;29(6):505-514.
11. Howard LM, Molyneaux E, Dennis C-L, Rochat T, Stein A, Milgrom J. Non-psychotic mental disorders in the perinatal period. The Lancet. 2014;384(9956):1775-1788.
12. Peltzer K, Rodriguez VJ, Jones D. Prevalence of prenatal depression and associated factors among HIV-positive women in primary care in Mpumalanga province, South Africa. SAHARA J. 2016;13(1):60-67.
13. Chaudoir SR, Fisher JD, Simoni JM. Understanding HIV disclosure: a review and application of the Disclosure Processes Model. Soc Sci Med. 2011;72(10):1618-1629.
14. Seth P, Kidder D, Pals S, Parent J, Mbatia R, Chesang K, et al. Psychosocial functioning and depressive symptoms among HIV-positive persons receiving care and treatment in Kenya, Namibia, and Tanzania. Prev Sci. 2014;15:318-328.

15. Shacham E, Small E, Onen N, Stamm K, Overton ET. Serostatus disclosure among adults with HIV in the era of HIV therapy. AIDS Patient Care STDS. 2012;26(1):29-35.
16. Farley J, Miller E, Zamani A, Tepper V, Morris C, Oyegunle M, et al. Screening for hazardous alcohol use and depressive symptomatology among HIV-infected patients in Nigeria: prevalence, predictors, and association with adherence. J Int Assoc Physicians AIDS Care. 2010;9(4):218-226.
17. Vyavaharkar M, Moneyham L, Corwin S, Tavakoli A, Saunders R, Annang L. HIV-disclosure, social support, and depression among HIV-infected African American women living in the rural southeastern United States. AIDS Educ Prev. 2011;23(1):78-90.
18. Daskalopoulou M, Lampe FC, Sherr L, Phillips AN, Johnson MA, Gilson R, et al. Non-disclosure of HIV status and associations with psychological factors, ART non-adherence, and viral load non-suppression among people living with HIV in the UK. AIDS Behav. 2017;21:184-195.
19. Mello VA, Segurado AA, Malbergier A. Depression in women living with HIV: clinical and psychosocial correlates. Arch Womens Ment Health. 2010;13:193-199.
20. Patel R, Ratner J, Gore-Felton C, Kadzirange G, Woelk G, Katzenstein D. HIV disclosure patterns, predictors, and psychosocial correlates among HIV positive women in Zimbabwe. AIDS Care. 2012;24(3):358-368.
21. Abler L, Sikkema KJ, Watt MH, Hansen NB, Wilson PA, Kochman A. Depression and HIV serostatus disclosure to sexual partners among newly HIV-diagnosed men who have sex with men. AIDS Patient Care STDS. 2015;29(10):550-558.
22. Ojikutu BO, Pathak S, Srithanaviboonchai K, Limbada M, Friedman R, Li S, et al. Community cultrual norms, stigma and disclosure to sexual partners among women living with HIV in Thailand, Brazil and Zambia (HPTN 063). PLoS ONE. 2016;11(5):e0153600.
23. Liu C, Goparaju L, Barnett A, Wang C, Poppen P, Young M, et al. Change in patterns of HIV status disclosure in the HAART era and association of HIV status disclosure with depression level among women. AIDS Care. 2017;29(9):1112-1118.
24. Cama E, Brener L, Slavin S, de Wit J. The relationship between negative responses to HIV status disclosure and psychosocial outcomes among people living with HIV. J Health Psychol. 2017: Epub ahead of print.
25. Medley AM, Kennedy CE, Lunyolo S, Sweat MD. Disclosure outcomes, coping strategies, and life changes among women living with HIV in Uganda. Qual Health Res. 2009;19(12):1744-1754.
26. Myer L, Phillips TK, Zerbe A, Ronan A, Hsiao N-Y, Mellins CA, et al. Optimizing antiretroviral therapy (ART) for maternal and child health (MCH): rationale and design of the MCH-ART study. J Acquir Immune Defic Syndr. 2016;72:S189-S196.
27. Myer L, Phillips TK, Zerbe A, Brittain K, Lesosky M, Hsiao N-Y, et al. Integration of postpartum healthcare services for HIV-infected women and their infants in South Africa: a randomised controlled trial. PLoS Med. 2018;15(3):e1002547.
28. Myer L, Phillips TK, Hsiao N-Y, Zerbe A, Petro G, Bekker L-G, et al. Plasma viraemia in HIV-positive pregnant women entering antenatal care in South Africa. J Int AIDS Soc. 2015;18:20045.
29. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2016.

30. Preciago J, Henry H. Linguistic barriers in health education and services. In: Garcia JG, Zea MC, editors. Psychological interventions and research with Latino populations. Boston: Allyn and Bacon; 1997.
31. Brittain K, Mellins CA, Phillips T, Zerbe A, Abrams EJ, Myer L, et al. Social support, stigma and antenatal depression among HIV-infected pregnant women in South Africa. AIDS Behav. 2017;21(1):274-282.
32. Brittain K, Mellins CA, Remien RH, Phillips T, Zerbe A, Abrams EJ, et al. Patterns and predictors of HIV-status disclosure among pregnant women in South Africa: dimensions of disclosure and influence of social and economic circumstances. AIDS Behav. 2018;22:3933-3944.
33. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987;150:782-786.
34. Murray D, Cox JL. Screening for depression during pregnancy with the Edinburgh Depression Scale (EDDS). J Reprod Infant Psychol. 1990;8(2):99-107.
35. Lawrie TA, Hofmeyr GJ, de Jager M, Berk M. Validation of the Edinburgh Postnatal Depression Scale on a cohort of South African women. S Afr Med J. 1998;88(10):1340-1344.
36. Ashaba S, Kaida A, Coleman JN, Burns BF, Dunkley E, O'Neil K, et al. Psychosocial challenges facing women living with HIV during the perinatal period in rural Uganda. PLoS ONE. 2017;12(5):e0176256.
37. Dima AL, Stutterheim SE, Lyimo R, de Bruin M. Advancing methodology in the study of HIV status disclosure: the importance of considering disclosure target and intent. Soc Sci Med. 2014;108:166-174.
38. Miller ES, Yee LM, Dorman RM, McGregor DV, Sutton SH, Garcia PM, et al. Is maternal disclosure of HIV serostatus associated with a reduced risk of postpartum depression? Am J Obstet Gynecol. 2016;215:521.e1-5.
39. Harrington BJ, Hosseinipour MC, Maliwichi M, Phulusa J, Jumbe A, Wallie S, et al. Prevalence and incidence of probable perinatal depression among women enrolled in Option B+ antenatal HIV care in Malawi. J Affect Disord. 2018;239:115-122.

Chapter 6: Long-term effects of unintended pregnancy on antiretroviral therapy outcomes among South African women living with HIV

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Author contributions

KB conceptualised and conducted the analysis, led data interpretation and drafted the manuscript. TKP and AZ directed data collection and assisted with data interpretation. EJA and LM conceptualised the study from which these data arise, were responsible for funding, implementation and overall leadership, and assisted with data interpretation. All authors read and approved the final manuscript.

Abstract

Objective: Unintended pregnancies are common among women living with HIV, but there are no data on their long-term impact on treatment outcomes. In a cohort of women initiating antiretroviral therapy (ART) during pregnancy, we examined the association between the intendedness of the current pregnancy, measured antenatally, and elevated viral load (VL) up to five years postpartum.

Design: Prospective study with enrolment at entry into antenatal care and follow-up at study visits separate from routine care.

Methods: At enrolment women completed the London Measure of Unplanned Pregnancy. Mixed effects models examined the impact of the intendedness of the pregnancy (planned versus each of unplanned or ambivalent, respectively) on VL ≥50 copies/mL across postpartum study visits.

Results: Overall, 459 women were followed for a median of 43 months postpartum, contributing 2535 VL measures (median per woman: 6). Ambivalent and unplanned pregnancy were commonly reported (20% and 60%, respectively), and the proportion of women with elevated VL increased over time (16% at 6 weeks to 43% by 36-60 months postpartum). Compared to those reporting a planned pregnancy, elevated VL was more common among women reporting an unplanned pregnancy [odds ratio (OR): 2.87; 95% confidence interval (CI): 1.46, 5.64], with a trend towards a higher odds among those reporting ambivalence (OR: 2.19; 95% CI: 0.97, 4.82); associations persisted after adjustment for a wide range of demographic, clinical and psychosocial factors.

Conclusions: These novel data suggest that unplanned pregnancy may be a prevalent and persistent predictor of poor ART outcomes among women initiating ART during pregnancy.

6.1 Introduction

Unintended pregnancies are a major public health concern, with global estimates suggesting that 44% of pregnancies were unintended in 2010-2014 [1]. In low- and middle-income country (LMIC) settings, unintended pregnancies are similarly prevalent: population-level surveys have reported that 65% of pregnancies during 2012 in South Africa [2] and 46% during 2001-2013 in Uganda were unplanned [3]; 69% of women in Swaziland have reported that their most recent pregnancy was unintended [4]. Outside the context of HIV, there are data to suggest that unintended pregnancy may be associated with a range of maternal health concerns [5] such as depression [6-9] or risk behaviours such as delayed initiation of antenatal care [5, 10, 11].

Despite the frequency of unintended pregnancy there have been few considerations of long-term effects among women living with HIV. In South Africa, fewer than 30% of pregnant women living with HIV report that their pregnancy was planned [12, 13], and experiencing an unintended pregnancy after being diagnosed HIV-positive is common in the United States [14, 15]. An unintended pregnancy may further heighten the psychosocial and economic vulnerabilities of pregnant women living with HIV [16, 17], and case-control studies have suggested that unintended pregnancies may be associated with mother-to-child HIV transmission [18, 19]. However, there are few data on the long-term effects on maternal and child outcomes.

In particular there has been no consideration of the long-term impact of an unintended pregnancy on maternal HIV treatment outcomes, including adherence to antiretroviral therapy (ART). The World Health Organization's policy of universal use of lifelong ART in all pregnant and breastfeeding women ('Option B+') [20] has contributed to major increases

in ART uptake but adherence to ART remains a major concern, particularly during the postpartum period [21-23]. Existing understandings of the drivers of suboptimal adherence in women living with HIV remain limited, including the potential role of unintended pregnancy. We have previously shown that unintended pregnancy is associated with elevated viral load (VL) at entry into antenatal care among women already on ART [24]. Here, we explored factors associated with the intendedness of the pregnancy among women who initiated ART during pregnancy; and examined the association between unintended pregnancy and elevated VL through 36-60 months postpartum.

6.2 Methods

6.2.1 Study design

We recruited consecutive pregnant women living with HIV from a public sector antenatal clinic in Gugulethu, Cape Town, for the MCH-ART study (ClinicalTrials.gov NCT01933477). The design and primary results of the study have been previously described [25, 26]. In this setting, women receive integrated PMTCT services and antenatal care within the broader maternal and child health care platform during pregnancy. Women who were eligible to initiate ART were followed through delivery. Women who then opted to breastfeed were randomised immediately postpartum to different models for delivering HIV care and were followed at repeated study measurement visits up to 18 months postpartum. Women were randomised to either the local standard of care (referral out of the maternal and child health clinic to general adult ART services at their 1st postpartum visit), or to the MCH-ART intervention of integrated concurrent and co-located maternal ART and paediatric care in the maternal and child health clinic through the end of breastfeeding. The trial found that there were significant improvements in the combined endpoint of viral suppression and retention in HIV care through 12 months postpartum among women randomised to the

intervention arm; retention in the MCH-ART trial did not differ across allocation [26]. We later extended follow-up to include one additional study visit between 36-60 months postpartum.

6.2.2 Participants

This secondary analysis includes all women who initiated ART during pregnancy and were followed as part of the randomised trial. ART eligibility was determined based on local guidelines: eligibility was based on CD4 cell count or clinical disease staging until June 2013, after which all pregnant women were ART-eligible under Option B+ guidelines. All women provided written informed consent prior to enrolment, and the study was approved by the University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee and by Columbia University Medical Center's Institutional Review Board.

6.2.3 Measures

Enrolment into the study coincided with women's entry into antenatal care. Women attended a maximum of two additional antenatal and one early postpartum study visit. Further study visits were then completed at 6 weeks and at 3, 6, 9, 12, 18 and 36-60 months postpartum, for a maximum of seven postpartum study visits. All study visits were completed separately from any routine HIV or antenatal/postpartum care.

Study measures based on self-report were administered in isiXhosa, the predominant local language, by trained study interviewers. Measures were translated from English into isiXhosa and were back-translated using standard procedures to ensure accuracy [27]. A composite poverty score was calculated based on employment, housing type and access to household resources [28]. At all study visits, women underwent phlebotomy for batched HIV VL testing

(Abbott RealTime HIV-1) conducted by the South African National Health Laboratory Services (NHLS). Infants underwent phlebotomy for HIV PCR testing at the 12 month study visit, conducted by the NHLS using the Roche Cobas AmpliPrep/Cobas TaqMan (CAP/CTM) HIV-1 assay (Roche diagnostics, New Jersey, USA).

The intendedness of the current pregnancy was assessed at enrolment, coinciding with entry into antenatal care, using the 6-item London Measure of Unplanned Pregnancy (LMUP) tool [29]. Each item was scored 0, 1 or 2, and all items were summed to create a score between 0 and 12, with higher scores indicating higher levels of intendedness; total scores were then categorised into unplanned (a score of 0-3), ambivalent (4-9) or planned pregnancy (10-12) [29]. The performance of the LMUP has been evaluated in both high-income and LMIC settings [30]. We have previously shown that the LMUP is a valid and reliable tool (Cronbach's alpha, 0.84) in pregnant women living with and without HIV in South Africa [13].

The Edinburgh Postnatal Depression Scale (EPDS) [31] was administered at participants' second antenatal study visit and at 6 weeks and 12, 18 and 36-60 months postpartum. A score of ≥13 was used to indicate elevated depressive symptoms [31]. The Alcohol Use Disorders Identification Test (AUDIT) [32] was administered at participants' 2nd antenatal study visit to assess alcohol use in the year prior to pregnancy recognition, and at 6, 12 and 36-60 months postpartum to assess postpartum alcohol use. In analysis, the AUDIT-C (AUDIT-Consumption) scoring system was used, where a score ≥3 on the first 3 items of the tool was used to indicate risky alcohol use [33, 34]. The World Health Organization Violence Against Women tool was used to assess intimate partner violence [35]. Violence in the year prior to pregnancy recognition was assessed at participants' 2nd antenatal study visit, and postpartum

violence was assessed at 12 and 36-60 months postpartum. In analysis, we categorised women as reporting any versus no violence.

6.2.4 Data analysis

Data were analysed using Stata 14 (StataCorp Inc, College Station, Texas, USA). We used mixed effects models to examine the impact of the intendedness of the pregnancy on elevated VL ≥50 copies/mL during the postpartum period. Throughout, we compared women reporting each of ambivalence or an unplanned pregnancy, respectively, to those reporting a planned pregnancy; and also examined the effect of increasing intendedness of the pregnancy using continuous LMUP scores. We conducted sensitivity analyses using (i) VL ≥1000 copies/mL and (ii) restricted to women who were virally suppressed <50 copies/mL at delivery. We explored the impact of missing data by assuming that women who did not attend a study visit had (i) suppressed and then (ii) elevated VL at that visit.

Given the potential for confounding of the putative association between the intendedness of the pregnancy and elevated VL we present results from unadjusted models and then: (A) adjusting for demographic and clinical characteristics only; (B) additionally adjusting for psychosocial factors measured at participants' second antenatal study visit; and (C) additionally adjusting for postpartum psychosocial factors. To account for differences in viral suppression at 12 months postpartum observed in the primary trial analysis, all adjusted models were adjusted for women's allocation in the MCH-ART trial. For postpartum psychosocial factors, we categorised women as scoring above the threshold value at any study visit at which these were assessed versus scoring below threshold at all visits. Possible modifiers of the association between the intendedness of the pregnancy and postpartum VL were examined in stratified analyses. Using standard formulae and assuming that unplanned

pregnancy is an independent cause of elevated VL for these purposes, we calculated the population attributable fraction for the proportion of elevated VL that may be due to unplanned pregnancy. Finally, we used product-limit methods and the log-rank test to compare vertical transmission across LMUP categories.

6.3 Results

6.3.1 Intendedness of the pregnancy

A total of 471 women who had initiated ART during pregnancy and opted to breastfeed were followed postpartum. Seven women had not completed the LMUP and were excluded from analysis; a further five women attended no follow-up visits and were excluded. The remaining 459 women were enrolled while pregnant between March 2013-April 2014. Approximately two-thirds of women reported that they were not using contraception during the month prior to the pregnancy; had not discussed getting pregnant with their partner; and did not want a baby or intend to get pregnant (Table 6.1). However, 49% of women who reported not wanting a baby and not intending to get pregnant, respectively, reported that the timing of the pregnancy was okay, although not quite right. Using the LMUP tool, 20%, 20% and 60% of women reported that their current pregnancy was intended, ambivalent and unplanned, respectively.

Table 6.1 Responses to London Measure of Unplanned Pregnancy tool

Variable	*n* (%)
Number of women	459
In the month that I became pregnant…	
I/we were not using contraception	315 (69)
I/we were using contraception, but not on every occasion	88 (19)
I/we always used contraception, but knew that the method had failed at least once	49 (11)
I/we always used contraception	7 (2)
In terms of becoming a mother, I feel that my pregnancy happened at the…	
Right time	146 (32)
Okay, but not quite right time	173 (38)
Wrong time	140 (31)
Just before I became pregnant…	
I intended to get pregnant	129 (28)
My intentions kept changing	34 (7)
I did not intend to get pregnant	296 (64)
Just before I became pregnant…	
I wanted to have a baby	131 (29)
I had mixed feelings about having a baby	36 (8)
I did not want to have a baby	292 (64)
Before I became pregnant…	
My partner and I had agreed that we would like me to be pregnant	124 (27)
My partner and I had discussed having children together, but hadn't agreed for me to get pregnant	29 (6)
We never discussed having children together	306 (67)
Actions to improve health in preparation for pregnancy[1]	
None	414 (90)
One	8 (9)
Two or more	4 (0.9)
LMUP score – median [IQR]	3 [2, 9]
Unplanned	275 (60)
Ambivalent	91 (20)
Planned	93 (20)

[1] Actions could include taking folic acid; stopping/cutting down on smoking or drinking alcohol; eating more healthily; seeking medical advice; or other actions

6.3.2 Demographic, clinical and psychosocial characteristics

Overall the median age was 27.9 years, and women had entered antenatal care at a median gestation of 21 weeks (Table 6.2). Women reported low levels of educational attainment and employment; 83% reported one or more previous pregnancies; and 58% were diagnosed HIV-positive during their current pregnancy. Psychosocial risk factors were commonly reported; 61% had disclosed their HIV status to their male partner by delivery; and 75% were virally suppressed <50 copies/mL at delivery. Women reporting lower levels of intendedness related to their current pregnancy were significantly less likely to be married and/or cohabiting; had entered antenatal care at a later gestation with consequent ART initiation at a later gestation; and were somewhat less likely to have VL <50 copies/mL at delivery. In addition, women reporting lower levels of intendedness were more likely to report risky alcohol use prior to pregnancy and during the postpartum period and were less likely to disclose to their male partner by delivery. No differences in intendedness of the pregnancy were observed by age; timing of HIV diagnosis (before versus during the pregnancy); or allocation in the MCH-ART trial.

Table 6.2 Demographic, clinical and psychosocial characteristics by the intendedness of the pregnancy

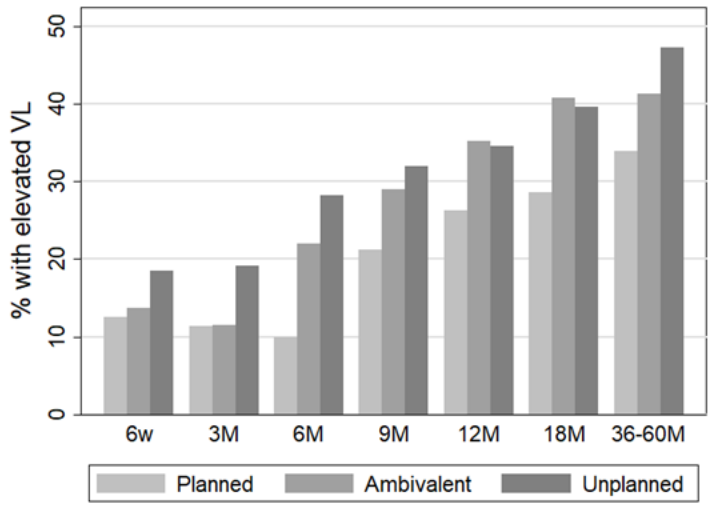
Variable[1]	Total – n (%)	Unplanned – n (%)	Ambivalent – n (%)	Planned – n (%)	*P*-value
Number of women	459	275	91	93	
Median [IQR] age	27.9 [24.5, 32.6]	27.7 [24.3, 32.3]	27.8 [24.9, 31.9]	28.9 [24.6, 33.0]	0.600
Completed secondary/any tertiary education	113 (25)	66 (24)	19 (21)	28 (30)	0.324
Employed	175 (38)	99 (36)	41 (45)	35 (38)	0.303
Married and/or cohabiting	189 (41)	87 (32)	35 (38)	67 (72)	<0.001
Timing of HIV diagnosis					
Before this pregnancy	194 (42)	117 (43)	39 (43)	38 (41)	
During this pregnancy	265 (58)	158 (57)	52 (57)	55 (59)	0.953
Previous antiretroviral use	125 (27)	80 (29)	26 (29)	19 (20)	0.255
First pregnancy	78 (17)	48 (17)	11 (12)	19 (20)	0.305
Median [IQR] gestation in weeks at entry into antenatal care	21 [16, 26]	22 [17, 28]	20 [14, 24]	19 [15, 24]	0.003
Median [IQR] CD4 cell count at entry into antenatal care	353 [247, 527]	346 [245, 534]	400 [273, 565]	345 [223, 493]	0.135
Median [IQR] HIV viral load at entry into antenatal care (log_{10} copies/mL)	4.0 [3.4, 4.6]	4.0 [3.4, 4.5]	4.0 [3.3, 4.6]	4.1 [3.3, 4.7]	0.847
Gestation at ART initiation					
<14 weeks	67 (15)	32 (12)	19 (21)	16 (17)	
14-27 weeks	279 (61)	162 (59)	52 (57)	65 (70)	
≥28 weeks	113 (25)	81 (29)	20 (22)	12 (13)	0.007
Antenatal depression: EPDS score ≥13	45 (10)	31 (11)	8 (9)	6 (6)	0.374
Risky alcohol use prior to pregnancy: AUDIT-C score ≥3	115 (25)	78 (28)	23 (26)	14 (15)	0.036
Any intimate partner violence prior to pregnancy	102 (22)	66 (24)	18 (20)	18 (19)	0.512
HIV viral load at delivery					
<50 copies/mL	346 (75)	198 (72)	73 (80)	75 (81)	
50-999 copies/mL	83 (18)	52 (19)	15 (16)	16 (17)	
≥1,000 copies/mL	30 (7)	25 (9)	3 (3)	2 (2)	0.090
Disclosed to male partner by delivery	282 (61)	164 (60)	50 (55)	68 (73)	0.025
Postpartum depression: EPDS score ≥13 at any timepoint	59 (13)	33 (12)	17 (19)	9 (10)	0.151
Risky postpartum alcohol use: AUDIT-C score ≥3 at any timepoint (*n*=439)	99 (23)	66 (25)	22 (24)	11 (13)	0.047
Any postpartum intimate partner violence reported at any timepoint (*n*=424)	49 (12)	31 (12)	8 (9)	10 (12)	0.764

[1] EPDS: Edinburgh Postnatal Depression Scale; AUDIT-C: Alcohol Use Disorders Identification Test – Consumption

6.3.3 Impact of the intendedness of the pregnancy on postpartum VL

Women were followed for a median of 42.6 months postpartum, contributing a total of 2535 VL measures [median per woman: 6; inter-quartile range (IQR): 5-7]. The proportion of women with VL ≥50 copies/mL increased from 16% at 6 weeks postpartum to 43% by 36-60 months postpartum. Overall, 56% of women had VL ≥50 copies/mL at one or more postpartum study visit. At most visits, a dose-response association was observed: elevated VL was more common among women who had reported ambivalence compared to a planned pregnancy, with the prevalence of elevated VL even higher among those who had reported that their pregnancy was unplanned (Figure 6.1). VL ≥50 copies/mL at one or more postpartum study visit was observed among 60% of women who reported that their pregnancy was unplanned, 62% of women who reported ambivalence, and 41% of women who reported that their pregnancy was planned.

Figure 6.1 Proportion with elevated viral load (VL) ≥50 copies/mL at postpartum timepoints[1] by intendedness of the pregnancy



[1] Postpartum timepoints: 6 weeks and 3, 6, 9, 12, 18 and 36-60 months postpartum.

In unadjusted analyses, lower levels of intendedness were associated with elevated VL at postpartum study visits: compared to women who had reported a planned pregnancy, those who had reported an unintended pregnancy had almost 3 times the odds [odds ratio (OR): 2.87; 95% confidence interval (CI): 1.46, 5.64] of elevated VL across study visits, with a trend towards a higher odds among those reporting ambivalence (OR: 2.19; 95% CI: 0.97, 4.92; Table 6.3). Elevated VL was also more common among women who were younger; were neither married nor cohabiting; had entered antenatal care at a later gestation and with higher VL; and reported risky pre-conception alcohol use or intimate partner violence. In addition, the odds of elevated VL increased with increasing duration on ART, and elevated VL was more common among women reporting risky alcohol use or intimate partner violence during the postpartum period.

The effect of the intendedness of the pregnancy on elevated VL persisted after adjustment for demographic and clinical characteristics (adjusted model A); additional adjustment for pre-conception and antenatal psychosocial factors (B); and after additional adjustment for postpartum psychosocial factors (C), although the associations did not reach statistical significance in all instances. Results were similar when elevated VL was defined as ≥1000 copies/mL and when models were restricted to women who were virally suppressed <50 copies/mL at delivery (data not shown) but were slightly attenuated when assuming that missing VL measures were (i) suppressed or (ii) elevated (Table S6.1).

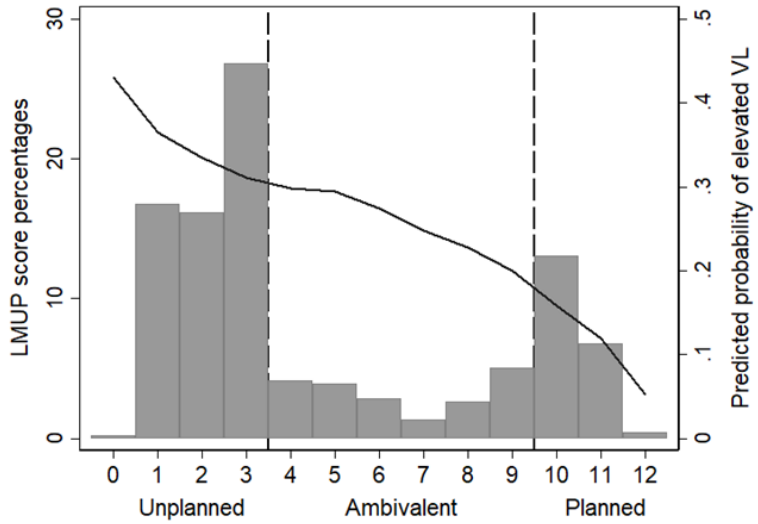
Table 6.3 Associations between the intendedness of the pregnancy and elevated viral load (VL) ≥50 copies/mL postpartum from unadjusted models, and after adjustment for (A) demographic and clinical factors; and additional adjustment for (B) baseline and (C) postpartum psychosocial factors

	Unadjusted models		Adjusted model A		Adjusted model B		Adjusted model C	
Variable[1]	OR [95% CI][2]	*P*-value	aOR [95% CI][3]	*P*-value	aOR [95% CI]	*P*-value	aOR [95% CI]	*P*-value
LMUP category (versus Planned)								
Ambivalent	**2.19 [0.97, 4.92]**	**0.058**	**1.72 [0.73, 4.05]**	**0.217**	**1.72 [0.73, 4.05]**	**0.214**	**1.56 [0.65, 3.76]**	**0.322**
Unplanned	**2.87 [1.46, 5.64]**	**0.002**	**1.97 [0.94, 4.14]**	**0.074**	**1.86 [0.89, 3.89]**	**0.099**	**1.73 [0.81, 3.69]**	**0.156**
Age	0.91 [0.87, 0.95]	<0.001	0.91 [0.86, 0.95]	<0.001	0.90 [0.86, 0.95]	<0.001	0.90 [0.85, 0.94]	<0.001
Poverty score	1.02 [0.81, 1.27]	0.893	1.09 [0.86, 1.37]	0.484	1.08 [0.86, 1.37]	0.506	1.08 [0.84, 1.38]	0.534
Married and/or cohabiting (versus neither married nor cohabiting)	0.45 [0.27, 0.75]	0.002	0.69 [0.39, 1.24]	0.216	0.71 [0.39, 1.28]	0.259	0.78 [0.42, 1.44]	0.431
Diagnosed HIV-positive during this pregnancy (versus before)	0.82 [0.49, 1.36]	0.444						
Previous antiretroviral use (versus no previous use)	1.68 [0.96, 2.94]	0.068	2.03 [1.12, 3.66]	0.019	2.02 [1.12, 3.64]	0.020	2.00 [1.10, 3.64]	0.023
Reports one or more previous pregnancies (versus first pregnancy)	0.70 [0.36, 1.37]	0.297						
Log_{10} VL at entry into antenatal care	1.63 [1.24, 2.14]	<0.001	1.76 [1.32, 2.35]	<0.001	1.78 [1.33, 2.38]	<0.001	1.73 [1.28, 2.33]	<0.001
Gestation at ART initiation in weeks	1.06 [1.03, 1.10]	<0.001	1.08 [1.04, 1.12]	<0.001	1.07 [1.03, 1.11]	<0.001	1.07 [1.03, 1.11]	0.001
Months on ART at VL assessment	1.06 [1.05, 1.07]	<0.001	1.06 [1.05, 1.07]	<0.001	1.06 [1.05, 1.07]	<0.001	1.06 [1.05, 1.07]	<0.001
Disclosed to male partner by delivery (versus did not disclose)	0.72 [0.43, 1.21]	0.216						
Antenatal depression	1.37 [0.58, 3.22]	0.472			0.64 [0.26, 1.57]	0.329	0.65 [0.26, 1.64]	0.363
Risky pre-conception alcohol use	1.80 [1.02, 3.20]	0.043			1.06 [0.57, 1.98]	0.846	0.95 [0.49, 1.87]	0.891
Any pre-conception intimate partner violence	2.93 [1.63, 5.28]	<0.001			2.81 [1.49, 5.31]	0.001	2.17 [1.12, 4.20]	0.022
Postpartum depression	1.98 [0.96, 4.11]	0.065					1.37 [0.61, 3.09]	0.446
Risky postpartum alcohol use	2.66 [1.48, 4.81]	0.001					1.73 [0.86, 3.47]	0.124
Any postpartum intimate partner violence	2.66 [1.23, 5.78]	0.013					2.23 [0.95, 5.19]	0.064

[1] LMUP: London Measure of Unplanned Pregnancy; depression defined as Edinburgh Postnatal Depression Scale (EPDS) score ≥13; risky alcohol use defined as Alcohol Use Disorders Identification Test – Consumption (AUDIT-C) score ≥3; [2] OR: odds ratio; 95% CI: 95% confidence interval; [3] aOR: adjusted odds ratio; All adjusted models adjusted for all covariates shown and for design effect

Results were consistent when examining the effect of continuous LMUP scores: increasing intendedness of the pregnancy was strongly associated with a reduced odds of elevated VL in unadjusted models, with associations only slightly attenuated in adjusted models (Table S6.2). In a graphical portrayal of LMUP scores and the predicted probability of experiencing elevated VL at each score (Figure 6.2), the magnitude of these results is clearly seen. First, the distribution of LMUP scores is bimodal, but the majority of women fall within the range of an unplanned pregnancy. Second, the highest probability of elevated VL falls in the large group of women who reported that their pregnancy was unintended, and the probability decreases in a dose-response relationship as the intendedness of the pregnancy increases.

Figure 6.2 Distribution of London Measure of Unplanned Pregnancy (LMUP) scores[1], with predicted probability of elevated viral load (VL) ≥50 copies/mL at postpartum study visits



[1] Higher score represents increasing intendedness of the pregnancy

6.3.4 Impact of the intendedness of the pregnancy across subgroups

The association between continuous LMUP scores and elevated VL ≥50 copies/mL was examined across subgroups (Figure S6.1). Overall, increasing intendedness of the pregnancy reduced the relative odds of elevated VL in most subgroups explored. However, this effect appeared to be stronger among women who had completed less than secondary education and who reported more disadvantage. In addition, the effect was stronger among women who were married and/or cohabiting and who reported no previous pregnancies. Although HIV-status disclosure to a male partner was not associated with elevated VL in the total sample (Table 6.3), the effect of the intendedness of the pregnancy on elevated VL appeared to be stronger among women who had disclosed to their male partner by delivery.

The role of HIV-status disclosure to a male partner was further explored in stratified analyses (Table S6.2). Among women who had not disclosed to their male partner by delivery, the intendedness of the pregnancy was not associated with elevated VL in either unadjusted or adjusted models. Among women who had disclosed by delivery, increasing intendedness of the pregnancy was strongly associated with a reduced odds of elevated VL (OR: 0.85; 95% CI: 0.77, 0.94); this effect persisted after adjustment for demographic and clinical factors but was slightly attenuated after additional adjustment for antenatal and postpartum psychosocial factors.

6.3.5 Impact of the intendedness of the pregnancy on vertical transmission

A total of 466 infants were born to the 459 women included in analysis, with 5 infants testing HIV-positive in the first 12 months postpartum. The rate of transmission at 12 months postpartum was 1.2% overall, with no difference across LMUP categories (p=0.999).

6.4 Discussion

This analysis presents novel data suggesting that unplanned pregnancy may be a common and persistent risk factor for poor ART outcomes among women initiating ART during pregnancy. We observed a dose-response association between lower levels of pregnancy intendedness and elevated VL, with elevated VL most common among women who had reported an unplanned pregnancy. This association persisted up to 36-60 months postpartum and was observed independent of demographic, clinical and psychosocial factors. To our knowledge, these data are the first to demonstrate a long-term effect of the intendedness of a pregnancy on VL and, given the high frequency of unintended pregnancy in women living with HIV in many LMIC settings, make an important new contribution to our understanding of the drivers of suboptimal adherence during the postpartum period.

Unintended pregnancies have been previously linked to other adverse health behaviours including delays in seeking antenatal care [5, 11, 36-38], substance use during pregnancy [36, 37], and lower levels of breastfeeding [5]. Further, the psychosocial consequences may be profound: an unintended pregnancy can cause severe disruption to pre-existing life plans [36] and may lead to common mental disorders such as depression [5, 7, 36, 38] as well as relationship dissolution or intimate partner violence [5, 36]. Our finding that unintended pregnancy affects maternal ART outcomes extends these findings to the biomedical outcomes of HIV treatment, viral suppression. Preventing unintended pregnancies is a central aspect of the approach to reduce vertical HIV transmission [39]; further, our data suggest that an unintended pregnancy may compromise the benefits of ART for maternal health in the long term.

Although the impact of pregnancy intention persisted despite adjustment for multiple other risk factors, direct causality is difficult to determine [5]. Unintended pregnancies occur in complex social contexts and relationships [37], including being more common among unmarried women [36], and may heighten existing vulnerabilities [16, 17]. It is likely that an unintended pregnancy is one of several risk factors that contribute to women's vulnerability, rather than a standalone factor that independently predicts elevated VL. Indeed, both the intendedness of a pregnancy and subsequent health outcomes may be determined by the same underlying factors [5]. In this study, several factors were associated with both lower levels of pregnancy intendedness and elevated VL: each was more common among women who were neither married nor cohabiting; had entered antenatal care at a later gestation; and who reported risky alcohol use. Here we posit that an unintended pregnancy heightens women's vulnerability as part of a constellation of risk factors. In addition, we posit that unintended pregnancy may be a marker of some degree of ambivalence both towards pregnancy and towards one's own health, with these ambivalences reflected in women's adherence to ART. Additional socio-behavioural research is needed to explore these possibilities and the mechanisms of these novel findings.

If unplanned pregnancy can be viewed as an independent cause of elevated VL for the purpose of considering population-level impacts, then it is possible to calculate a population attributable fraction for the proportion of elevated VL in the cohort that may be due to unplanned pregnancy. Using standard formulae, we estimate that approximately 16% of elevated VL may be associated with unplanned pregnancy in this population, compared to either ambivalence or a planned pregnancy; if we include ambivalence to pregnancy in the calculations this estimate increases to 28%. Given that unintended pregnancies are preventable (for example through effective contraception), an alternate way to conceptualise

this is to consider the possibility that only women with planned pregnancies entered the cohort. In this case, we estimate that 64% and 85% of all episodes of elevated VL would be prevented by the prevention of unplanned, or unplanned and ambivalent, pregnancies, respectively. Regardless of the formula used, these estimates speak to the population-level implications of the associations observed here.

A strength of this study is the inclusion of longitudinal data with long-term follow-up and the use of a robust biological endpoint. However, our results must be interpreted in light of several limitations. Unintended pregnancy is a complex construct to measure [37, 38] but the LMUP has been validated widely, including in this population [13], and is robust enough to be recommended as an outcome measure for preconception care [40]. We assessed the intendedness of the pregnancy at entry into antenatal care, but the desirability of the pregnancy may change during the course of pregnancy [5]. Indeed, we did not assess how quickly women adapted in psychosocial terms to the pregnancy but note that 49% of women who reported not wanting a baby and not intending to get pregnant, respectively, reported that the timing of the pregnancy was okay. Preconception measurement of pregnancy intentions would be ideal but is challenging. As these data arise from a peri-urban setting in South Africa in the context of a research study, our findings should be generalised to other settings with caution, but we note that high levels of both unplanned pregnancy and elevated VL have been observed in many high-burden settings [3, 4, 21-23]. Finally, this research focussed on women initiating ART in pregnancy, and the question of how unplanned pregnancy effects outcomes among women who initiated ART before conception needs further investigation.

Despite these limitations, these results clearly warrant further attention. Given the high levels of unintended pregnancy and elevated postpartum VL observed here and in other settings, we

argue that unintended pregnancy needs to be escalated as a global public health concern for maternal and child health in the context of HIV. Moreover, these data shed light on a unique factor in this patient population that may shape adherence behaviours and suggest that postpartum women who report antenatally that they did not intend their pregnancy may require specific attention from counselling and support interventions. Further, we argue that pregnancy planning needs to be incorporated into routine care for all women living with HIV: preventing unintended pregnancies may reduce the prevalence of elevated VL in this population and maximise maternal health.

References

1. Bearak J, Popinchalk A, Alkema L, Sedgh G. Global, regional, and subregional trends in unintended pregnancy and its outcomes from 1990 to 2014: estimates from a Bayesian hierarchical model. Lancet Glob Health. 2018;6:e380-e389.
2. Wabiri N, Chersich M, Shisana O, Blaauw D, Rees H, Dwane N. Growing inequities in maternal health in South Africa: a comparison of serial national household surveys. BMC Pregnancy Childbirth. 2016;16:256.
3. Grilo SA, Song X, Lutalo T, Mullinax M, Mathur S, Santelli J. Facing HIV infection and unintended pregnancy: Rakai, Uganda, 2001-2013. BMC Womens Health. 2018;18(1):46.
4. Warren CE, Abuya T, Askew I, Integra Initiative. Family planning practices and pregnancy intentions among HIV-positive and HIV-negative postpartum women in Swaziland: a cross sectional survey. BMC Pregnancy Childbirth. 2013;13:150.
5. Gipson JD, Koenig MA, Hindin MJ. The effects of unintended pregnancy on infant, child, and parental health: a review of the literature. Stud Fam Plan. 2008;39(1):18-38.
6. Brittain K, Myer L, Koen N, Koopowitz S, Donald KA, Barnett W, et al. Risk factors for antenatal depression and associations with infant birth outcomes: results from a South African birth cohort study. Paediatr Perinat Epidemiol. 2015;29(6):505-514.
7. Fisher J, Cabral de Mello M, Patel V, Rahman A, Tran T, Holton S, et al. Prevalence and determinants of common perinatal mental disorders in women in low- and lower-middle-income countries: a systematic review. Bull World Health Organ. 2012;90(2):139G-149G.
8. Howard LM, Molyneaux E, Dennis C-L, Rochat T, Stein A, Milgrom J. Non-psychotic mental disorders in the perinatal period. The Lancet. 2014;384(9956):1775-1788.
9. Peltzer K, Rodriguez VJ, Jones D. Prevalence of prenatal depression and associated factors among HIV-positive women in primary care in Mpumalanga province, South Africa. SAHARA J. 2016;13(1):60-67.
10. Cheng D, Schwarz EB, Douglas E, Horon I. Unintended pregnancy and associated maternal preconception, prenatal and postpartum behaviors. Contraception. 2009;79:194-198.
11. Dibaba Y, Fantahun M, Hindin MJ. The effects of pregnancy intention on the use of antenatal care services: systematic review and meta-analysis. Reprod Health. 2013;10:50.
12. Adeniyi OV, Ajayi AI, Moyaki MG, Goon DT, Avramovic G, Lambert J. High rate of unplanned pregnancy in the context of integrated family planning and HIV care services in South Africa. BMC Health Serv Res. 2018;18(1):140.
13. Iyun V, Brittain K, Phillips TK, le Roux S, Mcintyre JA, Zerbe A, et al. Prevalence and determinants of unplanned pregnancy in HIV-positive and HIV-negative pregnant women in Cape Town, South Africa: a cross-sectional study. BMJ Open. 2018;8:e019979.
14. Rahangdale L, Stewart A, Stewart RD, Badell M, Levison J, Ellis P, et al. Pregnancy intentions among women living with HIV in the United States. J Acquir Immune Defic Syndr. 2014;65:306-311.

15. Sutton MY, Zhou W, Frazier EL. Unplanned pregnancies and contraceptive use among HIV- positive women in care. PLoS ONE. 2018;13(5):e0197216.
16. Crankshaw TL, Voce A, King RL, Giddy J, Sheon NM, Butler LM. Double disclosure bind: complexities of communicating an HIV diagnosis in the context of unintended pregnancy in Durban, South Africa. AIDS Behav. 2014;18:S53-S59.
17. Lewinsohn R, Crankshaw T, Tomlinson M, Gibbs A, Butler L, Smit J. "This baby came up and then he said, "I give up!": The interplay between unintended pregnancy, sexual partnership dynamics and social support and the impact on women's well-being in KwaZulu-Natal, South Africa. Midwifery. 2018;62:29-35.
18. Beyene GA, Dadi LS, Mogas SB. Determinants of HIV infection among children born to mothers on prevention of mother to child transmission program of HIV in Addis Ababa, Ethiopia: a case control study. BMC Infect Dis. 2018;18(1):327.
19. Mnyani CN, Simango A, Murphy J, Chersich M, McIntyre JA. Patient factors to target for elimination of mother-to-child transmission of HIV. Global Health. 2014;10:36.
20. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2016.
21. Ahmed S, Kim MH, Abrams EJ. Risks and benefits of lifelong antiretroviral treatment for pregnant and breastfeeding women: a review of the evidence for the Option B+ approach. Curr Opin HIV AIDS. 2013;8:474-489.
22. Nachega JB, Uthman OA, Anderson J, Peltzer K, Wampold S, Cotton MF, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. AIDS. 2012;26:2039-2052.
23. Ngarina M, Popenoe R, Kilewo C, Biberfeld G, Ekstrom AM. Reasons for poor adherence to antiretroviral therapy postnatally in HIV-1 infected women treated for their own health: experiences from the Mitra Plus study in Tanzania. BMC Public Health. 2013;13:450.
24. Brittain K, Remien RH, Mellins CA, Phillips TK, Zerbe A, Abrams EJ, et al. Determinants of suboptimal adherence and elevated HIV viral load in pregnant women already on antiretroviral therapy when entering antenatal care in Cape Town, South Africa. AIDS Care. 2018:30(12):1517-1523.
25. Myer L, Phillips TK, Zerbe A, Ronan A, Hsiao N-Y, Mellins CA, et al. Optimizing antiretroviral therapy (ART) for maternal and child health (MCH): rationale and design of the MCH-ART study. J Acquir Immune Defic Syndr. 2016;72:S189-S196.
26. Myer L, Phillips TK, Zerbe A, Brittain K, Lesosky M, Hsiao N-Y, et al. Integration of postpartum healthcare services for HIV-infected women and their infants in South Africa: a randomised controlled trial. PLoS Med. 2018;15(3):e1002547.
27. Preciago J, Henry H. Linguistic barriers in health education and services. In: Garcia JG, Zea MC, editors. Psychological interventions and research with Latino populations. Boston: Allyn and Bacon; 1997.
28. Brittain K, Mellins CA, Phillips T, Zerbe A, Abrams EJ, Myer L, et al. Social support, stigma and antenatal depression among HIV-infected pregnant women in South Africa. AIDS Behav. 2017;21(1):274-282.
29. Barrett G, Smith SC, Wellings K. Conceptualisation, development and evaluation of a measure of unplanned pregnancy. J Epidemiol Community Health. 2004;58:426-433.

30. Hall J, Barrett G, Mbwana N, Copas A, Malata A, Stephenson J. Understanding pregnancy planning in a low-income country setting: validation of the London measure of unplanned pregnancy in Malawi. BMC Pregnancy Childbirth. 2013;13:200.
31. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987;150:782-786.
32. Saunders JB, Aasland OG, Babor TG, De La Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project early detection of persons with harmful alcohol consumption - II. Addiction. 1993;88:791-804.
33. Bradley KA, Bush KR, Epler AJ, Dobie DJ, Davis TM, Sporleder JL, et al. Two brief alcohol-screening tests from the Alcohol Use Disorders Identification Test (AUDIT): validation in a female Veterans Affairs patient population. Arch Intern Med. 2003;163(7):821-829.
34. Bush K, Kivlahan DR, Mcdonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Arch Intern Med. 1998;158:1789-1795.
35. Garcia-Moreno C, Jansen HAFM, Ellsberg M, Heise L, Watts C. WHO multi-country study on women's health and domestic violence against women. Geneva; 2005.
36. Brown SS, Eisenberg L, editors. The best intentions: unintended pregnancy and the well-being of children and families. Washington: National Academy Press; 1995.
37. Santelli J, Rochat R, Hatfield-Timajchy K, Colley Gilbert B, Curtis K, Cabral R, et al. The measurement and meaning of unintended pregnancy. Perspect Sex Reprod Health. 2003;35(2):94-101.
38. Tsui AO, McDonald-Mosley R, Burke AE. Family planning and the burden of unintended pregnancies. Epidemiol Rev. 2010;32:152-174.
39. World Health Organization. PMTCT strategic vision 2010-2015: preventing mother-to-child transmission of HIV to reach the UNGASS and Millennium Development Goals. Geneva: World Health Organization; 2010.
40. Frayne DJ, Verbiest S, Chelmow D, Clarke H, Dunlop A, Hosmer J, et al. Health care system measures to advance preconception wellness: consensus recommendations of the clinical workgroup of the National Preconception Health and Health Care Initiative. Obstet Gynecol. 2016;127(5):863-872.

Table S6.1 Associations between the intendedness of the pregnancy and elevated viral load (VL) ≥50 copies/mL postpartum from unadjusted models, and after adjustment for (A) demographic and clinical factors; and additional adjustment for (B) baseline and (C) postpartum psychosocial factors; stratified by assumptions regarding missing viral load measures

	Unadjusted models		Adjusted model A		Adjusted model B		Adjusted model C	
Variable[1]	OR [95% CI][2]	*P*-value	aOR [95% CI][3]	*P*-value	aOR [95% CI][4]	*P*-value	aOR [95% CI][5]	*P*-value
Total sample								
LMUP category (versus Planned)								
Ambivalent	2.19 [0.97, 4.92]	0.058	1.72 [0.73, 4.05]	0.217	1.72 [0.73, 4.05]	0.214	1.56 [0.65, 3.76]	0.322
Unplanned	2.87 [1.46, 5.64]	0.002	1.97 [0.94, 4.14]	0.074	1.86 [0.89, 3.89]	0.099	1.73 [0.81, 3.69]	0.156
Assuming that all missing viral load measures were <50 copies/mL								
LMUP category (versus Planned)								
Ambivalent	2.12 [1.06, 4.21]	0.033	1.80 [0.92, 3.51]	0.085	1.76 [0.91, 3.41]	0.093	1.47 [0.75, 2.88]	0.261
Unplanned	2.35 [1.32, 4.16]	0.003	1.78 [1.00, 3.17]	0.049	1.69 [0.96, 2.98]	0.070	1.52 [0.85, 2.70]	0.157
Assuming that all missing viral load measures were ≥50 copies/mL								
LMUP category (versus Planned)								
Ambivalent	1.17 [0.69, 1.98]	0.570	1.17 [0.62, 2.22]	0.628	1.19 [0.63, 2.26]	0.593	1.30 [0.68, 2.46]	0.430
Unplanned	1.58 [1.03, 2.44]	0.037	1.50 [0.87, 2.58]	0.143	1.47 [0.85, 2.53]	0.163	1.49 [0.87, 2.58]	0.150

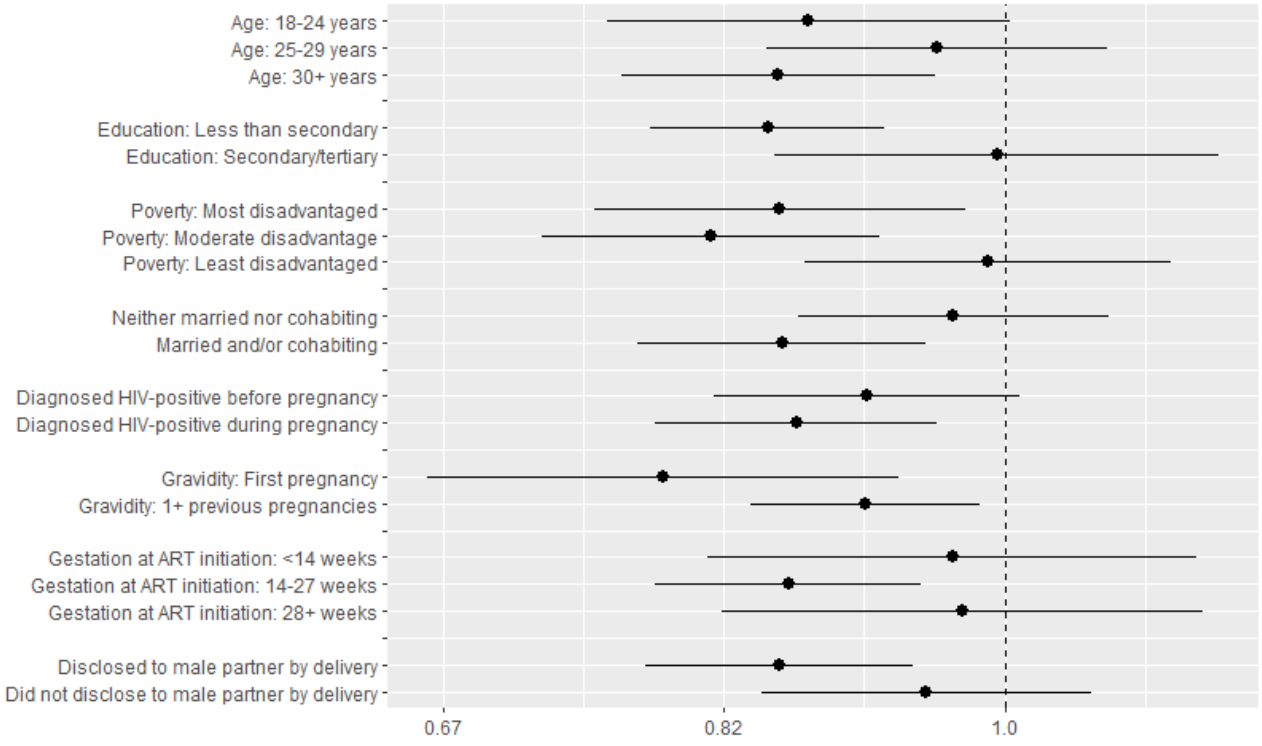
[1] LMUP: London Measure of Unplanned Pregnancy; [2] OR: odds ratio; 95% CI: 95% confidence interval; [3] aOR: adjusted odds ratio; model adjusted for age, socioeconomic status, marital status, previous antiretroviral use, $\log_{10}$ VL at entry into antenatal care, gestation at ART initiation, months on ART at VL assessment and design effect; [4] Model additionally adjusted for antenatal depression, risky pre-conception alcohol use and any pre-conception intimate partner violence; [5] Model additionally adjusted for postpartum depression, risky postpartum alcohol use and any postpartum intimate partner violence.

Table S6.2 Associations between the intendedness of the pregnancy and elevated viral load (VL) ≥50 copies/mL postpartum from unadjusted models, and after adjustment for (A) demographic and clinical factors; and additional adjustment for (B) baseline and (C) postpartum psychosocial factors; stratified by HIV-status disclosure to a male partner by delivery

	Unadjusted models		Adjusted model A		Adjusted model B		Adjusted model C	
Variable[1]	OR [95% CI][2]	*P*-value	aOR [95% CI][3]	*P*-value	aOR [95% CI][4]	*P*-value	aOR [95% CI][5]	*P*-value
Total sample								
LMUP score	0.88 [0.82, 0.95]	0.001	0.92 [0.85, 1.00]	0.054	0.93 [0.85, 1.00]	0.058	0.93 [0.85, 1.01]	0.074
Did not disclose to male partner by delivery								
LMUP score	0.95 [0.84, 1.06]	0.352	1.00 [0.88, 1.14]	0.990	1.00 [0.87, 1.14]	0.949	0.99 [0.86, 1.14]	0.909
Disclosed to male partner by delivery								
LMUP score	0.85 [0.77, 0.94]	0.001	0.89 [0.80, 0.99]	0.026	0.91 [0.82, 1.00]	0.061	0.92 [0.83, 1.02]	0.098

[1] LMUP: London Measure of Unplanned Pregnancy, with higher scores indicating greater intendedness of the pregnancy; [2] OR: odds ratio; 95% CI: 95% confidence interval; [3] aOR: adjusted odds ratio; model adjusted for age, socioeconomic status, marital status, previous antiretroviral use, $\log_{10}$ VL at entry into antenatal care, gestation at ART initiation, months on ART at VL assessment and design effect; [4] Model additionally adjusted for antenatal depression, risky pre-conception alcohol use and any pre-conception intimate partner violence; [5] Model additionally adjusted for postpartum depression, risky postpartum alcohol use and any postpartum intimate partner violence.

Figure S6.1 Odds ratios with 95% confidence intervals for the association between increasing intendedness of the pregnancy (one-unit increase in London Measure of Unplanned Pregnancy score) and elevated viral load ≥50 copies/mL postpartum, by subgroups



Chapter 7: Impact of HIV-status disclosure on HIV viral load during pregnancy and postpartum in Cape Town, South Africa

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Author contributions

KB conceptualised and conducted the analysis, led data interpretation and drafted the manuscript. TKP and AZ directed data collection and assisted with data interpretation. EJA and LM conceptualised the study from which these data arise, were responsible for funding, implementation and overall leadership, and assisted with data interpretation. CAM and RHR contributed to study design and assisted with data interpretation. All authors read and approved the final manuscript.

Abstract

Background: HIV-status disclosure is widely encouraged by counselling services, in part because it is thought to improve antiretroviral therapy (ART) adherence and thus HIV viral suppression. However, few longitudinal studies have examined the impact of disclosure on HIV viral load (VL) during pregnancy and postpartum.

Methods: We explored these associations among 1187 women living with HIV, enrolled between March 2013 and June 2014 in Cape Town, South Africa.

Results: Among women who tested HIV-positive before pregnancy, we observed no association between disclosure and VL at entry into antenatal care among those already on ART, nor at delivery and 12 months postpartum among those initiating ART. Among women who tested HIV-positive during pregnancy and initiated ART subsequently, disclosure to a male partner was associated with a reduced risk of VL ≥50 copies/mL at delivery [adjusted risk ratio (aRR): 0.56; 95% confidence interval (CI): 0.31, 1.01]. After stratification by relationship status, this association was only observed among women who were married and/or cohabiting. In addition, disclosure to ≥1 family/community member was associated with a reduced risk of VL ≥50 copies/mL at 12 months postpartum (aRR: 0.69; 95% CI: 0.48, 0.97) among newly-diagnosed women.

Conclusion: These findings suggest that the impact of disclosure on VL is modified by three factors: (i) timing of HIV diagnosis (before versus during the pregnancy); (ii) relationship to the person(s) to whom women disclose; and (iii) in the case of disclosure to a male partner, relationship status. Counselling about disclosure may be most effective if tailored to individual women's circumstances.

7.1 Introduction

Rapidly expanding access to antiretroviral therapy (ART) and universal initiation of lifelong ART for all pregnant and postpartum women (the World Health Organization's Option B+ approach) [1] have contributed to major increases in ART uptake and prevention of mother-to-child HIV transmission (PMTCT) [2-4]. Pregnancy represents a time-limited opportunity for the timely initiation of ART and promotion of optimal adherence which is imperative for both maternal and child health outcomes, including preventing vertical transmission. However, pregnant and postpartum women's adherence to ART remains a concern in many settings [5-7], thus limiting the benefits of ART for prevention and treatment.

HIV-status disclosure is widely believed to have beneficial impacts on ART adherence, as well as on factors such as social support and psychological well-being, and limited disclosure is a commonly cited barrier to adherence in the context of PMTCT [8-10]. Thus, disclosure to at least one person is routinely encouraged in counselling services. However, fears around disclosing among women living with HIV are widespread and include abandonment in the case of disclosing to a partner, and anticipated stigma in the case of disclosing to community members [11]. Further, some individuals experience negative reactions after disclosing [12, 13]. If disclosure does not improve adherence, then counselling services may be encouraging individuals to disclose when this may have negative repercussions. However, the current evidence for a beneficial effect of disclosure on adherence has limitations.

A major concern is that most studies to date have relied on cross-sectional data, making causality difficult to determine. Further, disclosure is a process that occurs over time, and it is plausible that the impact of disclosure may change over time. Notably, cross-sectional studies in numerous countries in Africa have found significant associations between disclosure and

adherence in the context of PMTCT [14-18], but significant associations are less frequently reported in longitudinal studies [19]. Prospective investigations are needed to provide high-quality evidence for the association between disclosure and adherence, as well as to explore the possibility of changes in this association over time.

Further limitations in this literature include a widespread reliance on self-reported adherence and few considerations of subgroups or differences in the effects of disclosure to different individuals. Self-reported adherence measures suffer from recall and social desirability biases [20], but few studies in the context of PMTCT have explored the impact of disclosure on HIV viral suppression, a more robust biological measure, a strong indication of ART adherence, and the ultimate goal of ART use. The few existing studies suggest that non-disclosure to a male partner is associated with elevated viral load (VL) at delivery in South Africa [21] and in France [22], and at approximately 4 years postpartum in Uganda [23]. However, only one of these studies assessed the impact of disclosure to family members on VL. We have previously shown that disclosure to male partners and to family/community members form separate dimensions, and that factors such as relationship status modify the associations between women's characteristics and disclosure [24]. It is plausible that disclosure to different individuals may have different effects on medication taking behaviours, and thus on VL, and that the effect of disclosure may differ in different subgroups, but these possibilities require further consideration.

There is an urgent need to help women maintain optimal adherence in order to achieve and maintain viral suppression during pregnancy and while breastfeeding, thereby minimising the risk of vertical transmission, and HIV-status disclosure may confer these benefits. Further investigations that use longitudinal data to explore the association between disclosure and VL

are clearly needed, as well as investigations of how disclosure in different subgroups and to different individuals may change this association. To address this gap, we explored the impact of disclosure on HIV VL among two groups of women in Cape Town, South Africa: (i) women already on ART when entering antenatal care, using cross-sectional analyses; and (ii) women initiating ART during pregnancy and followed through pregnancy and postpartum, using longitudinal data.

7.2 Methods

7.2.1 Study design

These analyses draw on a multi-phase implementation science study (the MCH-ART study) which evaluated strategies for delivering HIV care and treatment services during pregnancy and postpartum (ClinicalTrials.gov NCT01933477). The design, methods and primary findings of the study have been previously described [25, 26]. Briefly, the study was conducted at one antenatal care clinic in the former township of Gugulethu, and included a cross-sectional evaluation of pregnant women living with HIV who were entering antenatal care; an observational cohort study following women who initiated ART during the pregnancy through their first postpartum clinic visit (for up to three additional study visits); and an intervention study evaluating strategies for delivering HIV care to breastfeeding women during the postpartum period (for up to six additional study visits). ART eligibility was determined based on local guidelines: until June 2013, eligibility was determined based on CD4 cell count or clinical disease staging; from July 2013 onward, all pregnant women living with HIV were eligible to initiate lifelong ART under Option B+ guidelines.

7.2.2 Participants

For the broader MCH-ART study, consecutive pregnant women living with HIV who were entering antenatal care were recruited and enrolled; for the current analyses, women who had tested HIV-positive before the pregnancy and were already on ART were included in cross-sectional analyses. Women who initiated ART during the pregnancy were followed through delivery in the broader study, and women opting to breastfeed were followed through the postpartum period. For the current analyses, all women initiating ART and followed as part of the broader study were included in longitudinal analyses through 12 months (m) postpartum. All women provided written informed consent prior to enrolment, and the study was approved by the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee and by Columbia University Medical Center Institutional Review Board.

7.2.3 Measures

Study measures were administered by trained interviewers at study visits separate from routine HIV or antenatal/postpartum care. All measures were translated into and administered in isiXhosa, the predominant local language. Measures were back-translated prior to the study using standard procedures to ensure accuracy [27]. Basic sociodemographic characteristics were assessed at enrolment, and included age, educational attainment, relationship status and pregnancy intention. A composite poverty score was calculated based on current employment, housing type and access to household assets, as previously described [28]. Gestation was assessed using ultrasound. Women self-reported their date of HIV diagnosis and their date of ART initiation. Disclosure to male partners and to family/community members was assessed at all study visits. Family/community members included: mother; father; sister; brother; uncle; aunt; male cousin; female cousin; other male family member; other female family member; friend; and spiritual leader. This list was developed for the

purposes of this study. At each study visit, disclosure to each category was assessed using response options of 'Yes', 'No', or 'Not Applicable'. Given that our intention was to compare women who had disclosed to those who had not disclosed, either through deciding not to disclose to a specific individual or because this individual is not present in their life, we combined the response options 'No' and 'Not applicable' in analyses. CD4 enumeration via flow cytometry (Beckman Coulter) was conducted as part of routine care at entry into antenatal care, and women underwent phlebotomy at every study visit for batched HIV VL testing (Abbott RealTime HIV-1) conducted by the South African National Health Laboratory Services.

7.2.4 Data analysis

Data were analysed using Stata 12 (StataCorp Inc, College Station, Texas, USA). Throughout, we explored disclosure using two separate constructs: (i) disclosure to a male partner and (ii) disclosure to ≥1 family/community member, given that these disclosure events form separate dimensions in this sample [24]. We defined elevated VL as ≥50 copies/mL, and ≥1000 copies/mL in sensitivity analyses. Results were similar in sensitivity analyses, thus we present only results using ≥50 copies/mL.

Among women who had tested HIV-positive before the pregnancy and were established on ART, we examined the impact of disclosure on elevated VL at entry into antenatal care in logistic regression models. Among women initiating ART during pregnancy (including those who had tested HIV-positive before the pregnancy as well as those who tested HIV-positive during the pregnancy), we examined the impact of disclosure on elevated VL at (i) delivery and (ii) 12m postpartum in Poisson regression models with robust error variance [29]. For these analyses, we used cumulative reports of disclosure through delivery and 12m

postpartum, and stratified analyses by the timing of HIV diagnosis (before versus during the pregnancy). For the analyses of VL at delivery, we excluded women who had not been on ART >12 weeks (and >16 weeks in sensitivity analyses) in order to exclude women who may not have had a sufficient duration of ART use to reach viral suppression. Finally, we explored the impact of missing data by assuming that women who were lost from the study prior to delivery or 12m postpartum had (i) suppressed and (ii) elevated VL; these assumptions did not appreciably change the results.

7.3 Results

7.3.1 Sociodemographic and clinical characteristics

We included 1187 pregnant women living with HIV, enrolled between March 2013 and June 2014. A total of 559 women who had tested HIV-positive before the pregnancy and were already on ART at entry into antenatal care (median age: 31.5 years; median time since diagnosis: 4.6 years) were included in cross-sectional analyses. Data from 628 women who were initiating ART during the pregnancy (median age overall: 28.0 years; 56% diagnosed HIV-positive during the pregnancy) were included in longitudinal analyses.

Sociodemographic and clinical characteristics are described in Table 7.1. Low levels of married and/or cohabiting relationship status and intended pregnancy were observed in both groups. Overall, women had entered antenatal care at a median gestation of 20 weeks (inter-quartile range: 15-26 weeks).

Table 7.1 Demographic and clinical characteristics at entry into antenatal care, stratified by timing of HIV diagnosis and antiretroviral therapy (ART) use

			Initiating ART during pregnancy – *n* (%)	
Variable	Total sample – *n* (%)	Tested HIV-positive before pregnancy and on ART at entry into antenatal care – *n* (%)	Tested HIV-positive before pregnancy	Tested HIV-positive during pregnancy
Number of women	1187	559	276	352
Median [IQR] age	29.9 [26.0, 33.9]	31.5 [27.9, 34.9]	29.6 [26.3, 32.9]	26.9 [23.5, 31.6]
Educational attainment				
Less than secondary	896 (75)	434 (78)	219 (79)	243 (69)
Completed secondary/any tertiary	291 (25)	125 (22)	57 (21)	109 (31)
Currently employed	450 (38)	212 (38)	92 (33)	146 (41)
Poverty categories				
Most disadvantaged	431 (36)	204 (36)	103 (37)	124 (35)
Moderate disadvantage	399 (34)	191 (34)	92 (33)	116 (33)
Least disadvantaged	357 (30)	164 (29)	81 (29)	112 (32)
Married/cohabiting	530 (45)	271 (48)	129 (47)	130 (37)
First pregnancy	169 (14)	58 (10)	16 (6)	95 (27)
Pregnancy intentions				
Unintended	755 (64)	313 (56)	197 (71)	245 (70)
Intended	432 (36)	246 (44)	79 (29)	107 (30)
Median [IQR] gestation in weeks	20 [15, 26]	19 [14, 26]	20 [15, 25]	21 [16, 27]
Median [IQR] CD4 cell count	371 [259, 530]	403 [286, 541]	338 [228, 528]	352 [247, 504]
Median [IQR] years since diagnosis, among women who tested HIV-positive before pregnancy	4.3 [2.5, 7.0]	4.6 [2.9, 7.4]	3.8 [2.1, 6.1]	-

7.3.2 Women established on ART: impact of disclosure on VL

Among women already on ART at entry into antenatal care, 21% had an elevated VL ≥50 copies/mL (Table 7.2). Disclosure to a male partner was reported by 85% of women, and 95% had disclosed to ≥1 family/community member. Neither disclosure to a male partner nor disclosure to ≥1 family/community member was associated with VL in unadjusted or adjusted models. This lack of association persisted when models were stratified by relationship status and by age categories.

7.3.3 Women initiating ART: impact of disclosure on VL at delivery

Of 628 women who were initiating ART during the pregnancy, only 30 (5%) were lost from the study prior to delivery. Of the women retained at study measurement visits, 147 (25%) had not been on ART >12 weeks at delivery and were excluded from analysis, as they may not have had a sufficient duration of ART use to reach viral suppression. No differences in disclosure to a male partner were observed between those excluded versus those included (64% versus 65%; p=0.899; Table S7.1), but women who were excluded from analysis were less likely to have disclosed to ≥1 family/community member by delivery (64% versus 75%; p=0.013; Table S7.1).

Among women who tested HIV-positive before the pregnancy and who were included in analysis (20% with elevated VL ≥50 copies/mL at delivery), neither disclosure to a male partner nor disclosure to ≥1 family/community member was associated with elevated VL at delivery (Table 7.3). By delivery, 73% of this group had disclosed to their male partner, and 84% had disclosed to ≥1 family/community member. Among the women who tested HIV-positive during the pregnancy and who were included in analyses (21% with elevated VL ≥50 copies/mL at delivery), disclosure to ≥1 family/community member by delivery was not

associated with VL, but disclosure to a male partner was associated with a reduced risk of elevated VL at delivery. By delivery, 57% and 66% of this group had disclosed to a male partner and to ≥1 family/community member, respectively. The impact of disclosure to a male partner on VL persisted after adjustment [adjusted risk ratio (aRR): 0.56; 95% CI: 0.31, 1.01], and results were similar when restricted to women who had been on ART >16 weeks at delivery (aRR: 0.58; 95% CI: 0.26, 1.29). This impact appeared to be modified by relationship status: among women who were married and/or cohabiting, disclosure to a male partner was strongly associated with a reduced risk of elevated VL at delivery in adjusted models (aRR: 0.20; 95% CI: 0.08, 0.55), but no effect was observed among women who were neither married nor cohabiting (aRR: 0.80; 95% CI: 0.43, 1.49; *p*-value for interaction=0.006).

Table 7.2 Impact of disclosure on elevated viral load (VL, in copies/mL) at entry into antenatal care among women already on antiretroviral therapy (ART)

Variable	Total sample – *n* (%)	VL <50 – *n* (%)	VL ≥50 – *n* (%)	OR [95% CI][1]	*P*-value	aOR [95% CI][2]	*P*-value
Number of women	559	439	120				
Male partner disclosure							
Has not disclosed	83 (15)	63 (14)	20 (17)	Reference		Reference	
Has disclosed	476 (85)	376 (86)	100 (83)	0.84 [0.48, 1.45]	0.528	0.84 [0.48, 1.49]	0.558
Family/community disclosure							
Disclosed to none	30 (5)	24 (5)	6 (5)	Reference		Reference	
Disclosed to ≥1 person	529 (95)	415 (95)	114 (95)	1.10 [0.44, 2.75]	0.841	0.90 [0.35, 2.33]	0.827

[1] OR: odds ratio; [2] aOR: adjusted odds ratio; adjusted for age, poverty, relationship status, time since HIV diagnosis.

Table 7.3 Impact of disclosure on elevated viral load (VL, in copies/mL) at delivery among women initiating antiretroviral therapy (ART) during the pregnancy

Variable	Total sample – *n* (%)	VL <50 – *n* (%)	VL ≥50 – *n* (%)	RR [95% CI][1]	*P*-value	aRR [95% CI][2]	*P*-value
Tested HIV-positive before pregnancy							
Number of women	215	172	43				
Male partner							
Has not disclosed	59 (27)	50 (29)	9 (21)	Reference		Reference	
Has disclosed	156 (73)	122 (71)	34 (79)	1.43 [0.73, 2.80]	0.298	1.46 [0.75, 2.82]	0.261
Family/community							
Disclosed to none	35 (16)	28 (16)	7 (16)	Reference		Reference	
Disclosed to ≥1 person	180 (84)	144 (84)	36 (84)	1.00 [0.48, 2.07]	1.000	1.01 [0.48, 2.14]	0.973
Tested HIV-positive during pregnancy							
Number of women	236	187	49				
Male partner							
Has not disclosed	101 (43)	73 (39)	28 (57)	Reference		Reference	
Has disclosed	135 (57)	114 (61)	21 (43)	0.56 [0.34, 0.93]	0.025	0.56 [0.31, 1.01]	0.055
Family/community							
Disclosed to none	80 (34)	64 (34)	16 (33)	Reference		Reference	
Disclosed to ≥1 person	156 (66)	123 (66)	33 (67)	1.06 [0.62, 1.80]	0.837	0.82 [0.46, 1.47]	0.510

[1] RR: risk ratio; [2] aRR: adjusted risk ratio; adjusted for age, poverty, relationship status, pregnancy intention, $\log_{10}$ VL at entry into antenatal care, duration of ART use at delivery.

7.3.4 Women initiating ART: impact of disclosure on VL at 12m postpartum

Of 471 women who were breastfeeding and enrolled into postpartum follow-up, 60 women were excluded from analysis: 59 women (13%) were lost from the study, and one woman did not have a VL measure at 12m postpartum. Compared to women retained and with VL measures available, those excluded were significantly younger, had entered antenatal care at a later gestation, and were more likely to report that this was their first pregnancy and to have been diagnosed during the pregnancy; no differences in disclosure by the time of delivery were observed between those excluded from analysis and those retained (Table S7.2).

Among women diagnosed before the pregnancy and included in analyses (36% with elevated VL ≥50 copies/mL at 12m postpartum), no association between elevated VL and either disclosure to a male partner or disclosure to ≥1 family/community member was observed (Table 7.4). By 12m postpartum, disclosure to a male partner was reported by 74% of these women, and disclosure to ≥1 family/community member by 86%. Among women diagnosed during the pregnancy and included in analyses (32% with elevated VL ≥50 copies/mL at 12m postpartum), no association was observed between disclosure to a male partner and elevated VL, but disclosure to ≥1 family/community member appeared to reduce the risk of elevated VL at 12m postpartum in adjusted models (aRR: 0.69; 95% CI: 0.48, 0.97). By 12m postpartum, 60% of women in this group had disclosed to their male partner, and 73% had disclosed to ≥1 family/community member.

Table 7.4 Impact of disclosure on elevated viral load (VL, in copies/mL) at 12 months postpartum among women initiating antiretroviral therapy (ART) during the pregnancy

Variable	Total sample – *n* (%)	VL <50 – *n* (%)	VL ≥50 – *n* (%)	RR [95% CI][1]	*P*-value	aRR [95% CI][2]	*P*-value
Tested HIV-positive before pregnancy							
Number of women	183	118	65				
Male partner							
Has not disclosed	47 (26)	28 (24)	19 (29)	Reference		Reference	
Has disclosed	136 (74)	90 (76)	46 (71)	0.84 [0.55, 1.27]	0.406	0.78 [0.52, 1.17]	0.233
Family/community							
Disclosed to none	25 (14)	17 (14)	8 (12)	Reference		Reference	
Disclosed to ≥1 person	158 (86)	101 (86)	57 (88)	1.13 [0.61, 2.07]	0.700	1.18 [0.67, 2.09]	0.563
Tested HIV-positive during pregnancy							
Number of women	228	154	74				
Male partner							
Has not disclosed	91 (40)	61 (40)	30 (41)	Reference		Reference	
Has disclosed	137 (60)	93 (60)	44 (59)	0.97 [0.67, 1.43]	0.893	0.79 [0.56, 1.14]	0.209
Family/community							
Disclosed to none	62 (27)	38 (25)	24 (32)	Reference		Reference	
Disclosed to ≥1 person	166 (73)	116 (75)	50 (68)	0.78 [0.53, 1.15]	0.208	0.69 [0.48, 0.97]	0.035

[1] RR: risk ratio; [2] aRR: adjusted risk ratio; adjusted for age, poverty, relationship status, pregnancy intention, design effect, VL at delivery, duration of ART use at 12 months postpartum.

7.4 Discussion

In this sample of pregnant and postpartum women in South Africa, high levels of HIV-status disclosure were reported, however the association between disclosure and VL was complex. Disclosure did not appear to have an impact on VL at any time point assessed among women who tested HIV-positive before the pregnancy, including women who were established on ART and those initiating ART during the pregnancy. Yet among women who were newly diagnosed HIV-positive during the pregnancy and initiated ART, disclosure to a male partner appeared to be associated with a reduced risk of elevated VL at delivery, although this association was only observed among women who were married and/or cohabiting. In this group of women who tested HIV-positive during the pregnancy, we also observed an association between disclosure to ≥1 family/community member and a reduced risk of elevated VL at 12m postpartum. Altogether, though we observed high levels of both disclosure and viraemia in this cohort, non-disclosure does not appear to be a primary driver of elevated VL.

The few existing studies of the impact of disclosure to a male partner on viral suppression in the context of PMTCT suggest a beneficial effect [21-23]. Our findings suggest a more nuanced association: here, disclosure has a beneficial effect on viral suppression only among some women, and only in some circumstances. This is consistent with qualitative research suggesting that many women manage to maintain ART adherence regardless of non-disclosure [30]. Studies of the impact of disclosure on VL in adults living with HIV in Africa have yielded mixed results, with some showing that disclosure reduces the odds of virologic failure [31], others finding no association between disclosure and VL [32, 33], and still others showing higher levels of treatment failure among individuals reporting having disclosed [34]. Through our use of longitudinal data and nuanced disclosure measures, as well as our

consideration of subgroups, our results may help put these mixed findings into context. We propose that the impact of disclosure on VL is modified by three factors: (i) the timing of HIV diagnosis (before versus during the pregnancy); (ii) relationship to the person(s) to whom women disclose; and (iii) in the case of disclosure to a male partner, relationship status. We explore each of these proposed modifying factors below.

Significant associations between disclosure and adherence have been observed less frequently in longitudinal compared to cross-sectional research [19]. Here, we show that the impact of disclosure differs across the timing of HIV diagnosis, and across time points of assessment. Our results suggest that there is a critical window during which disclosure to a male partner helps newly-diagnosed women to establish optimal adherence behaviours. Women who are diagnosed HIV-positive during pregnancy face a triple burden: they must quickly adjust to the pregnancy, a new HIV diagnosis and the need to start lifelong ART [35], and barriers to ART adherence may be even more pronounced in this group [10]. Qualitative work in Uganda has suggested an evolution of coming to terms with an HIV diagnosis and developing coping strategies [36], and our results suggest that disclosure to a married or cohabiting male partner may be most beneficial during this critical window. Further, our results suggest that counselling should consider that the consequences of disclosure evolve over time [37].

The reasons for disclosing to different categories of people may differ [30, 38], and our results suggest that the impact of disclosing to different individuals may similarly differ. In previous research among pregnant women in South Africa, both disclosure to a male partner and disclosure to family members have been found to be associated with improved ART adherence [39], but different effects of disclosure to male partners and to family/community members on the use of PMTCT services have been demonstrated in Kenya [40]. Similarly,

disclosure to a partner has been shown to increase linkage to HIV care among males in Kenya, while disclosure to family members has increased linkage among females [41]. In the present study, disclosure to family/community members appeared to play a more important role in VL outcomes at 12m postpartum among newly-diagnosed women.

We observed an association between disclosure to a male partner and VL at delivery only among women who were married and/or cohabiting, suggesting that an individual's living situation may moderate both the patterns of disclosure and the consequences of disclosure [42]. Married and/or cohabiting relationship status is a well-documented predictor of disclosure to a male partner [43-46]; here, we demonstrate that relationship status additionally affects the impact of disclosure on VL. Disclosure to a male partner has been previously shown to only affect adherence to antiretrovirals for PMTCT under certain conditions [47] including, for example, delivering at home versus in a health facility [48]. For women who are neither married nor cohabiting with their partner, maintaining high levels of adherence may be easier due to the relative ease of secrecy around ART use. Alternatively, the mediating processes that happen as a result of disclosure, rather than the disclosure event alone, may be critical in affecting outcomes [49]; here, women in married and/or cohabiting relationships may be provided with greater support after disclosing, leading to improved outcomes, while non-disclosure may contribute to poorer ART outcomes.

A strength of the present study is the inclusion of longitudinal analyses, and the inclusion of a robust biological and clinical endpoint. We included a large sample recruited from a primary care antenatal clinic, and our findings are likely to be generalisable to other communities of pregnant and postpartum women in the region, although further research is needed to extrapolate our findings outside of the context of pregnancy. A limitation of this analysis is

that disclosure was assessed using self-report and may be subject to recall and social desirability bias, but this is common to all disclosure research. Thus, we used nuanced disclosure measures and extend the literature by assessing both disclosure to a male partner and to family/community members in analysis. We did not assess women's reports of individuals' reactions to disclosure, which may determine whether disclosure is beneficial [49, 50]. Women who were lost to follow-up were excluded from analysis, although we used sensitivity analyses to explore the impact of these missing data. Finally, a fairly large proportion of women (25%) did not have a sufficient duration of ART use and were excluded from analyses of VL at delivery. Our results from these analyses are thus restricted to women who had initiated ART earlier in the pregnancy.

Despite some limitations, these results are notable. Although disclosure may have other benefits, we argue that the widely-held belief that disclosure always has a beneficial impact on adherence needs to recognise that this relationship is more nuanced: disclosure may be beneficial for some women, at some time points, but these benefits are dependent on three critical factors: (i) the timing of HIV diagnosis (before versus during the pregnancy); (ii) relationship to the person(s) to whom women disclose; and (iii) in the case of disclosure to a male partner, relationship status. Further research is needed to explore the causality and mechanisms of these unique findings. We recommend that counselling about disclosure should ideally be tailored to individual women's circumstances, particularly during pregnancy and the postpartum period. While individualised counselling may not be feasible in busy primary care settings, our results suggest that there are particular subgroups, such as newly-diagnosed women, for whom tailored counselling around disclosure may be most beneficial.

References

1. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2016.
2. Abrams EJ, Myer L. Can we achieve an AIDS-free generation? Perspectives on the global campaign to eliminate new pediatric HIV infections. J Acquir Immune Defic Syndr. 2013;63:S208-S212.
3. Luzuriaga K, Mofenson LM. Challenges in the elimination of pediatric HIV-1 infection. N Engl J Med. 2016;374:761-770.
4. Mandelbrot L, Tubiana R, Le Chenadec J, Dollfus C, Faye A, Pannier E, et al. No perinatal HIV-1 transmission from women with effective antiretroviral therapy starting before conception. Clin Infect Dis. 2015;61(11):1715-1725.
5. Ahmed S, Kim MH, Abrams EJ. Risks and benefits of lifelong antiretroviral treatment for pregnant and breastfeeding women: a review of the evidence for the Option B+ approach. Curr Opin HIV AIDS. 2013;8:474-489.
6. Nachega JB, Uthman OA, Anderson J, Peltzer K, Wampold S, Cotton MF, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. AIDS. 2012;26:2039-2052.
7. Ngarina M, Popenoe R, Kilewo C, Biberfeld G, Ekstrom AM. Reasons for poor adherence to antiretroviral therapy postnatally in HIV-1 infected women treated for their own health: experiences from the Mitra Plus study in Tanzania. BMC Public Health. 2013;13:450.
8. O'Hiarlaithe M, Grede N, de Pee S, Bloem M. Economic and social factors are some of the most common barriers preventing women from accessing maternal and newborn child health (MNCH) and prevention of mother-to-child transmission (PMTCT) services: a literature review. AIDS Behav. 2014;18:S516-S530.
9. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. J Int AIDS Soc. 2013;16:18588.
10. Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J, et al. A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women PLoS ONE. 2014;9(11):e111421.
11. Ashaba S, Kaida A, Coleman JN, Burns BF, Dunkley E, O'Neil K, et al. Psychosocial challenges facing women living with HIV during the perinatal period in rural Uganda. PLoS ONE. 2017;12(5):e0176256.
12. King R, Katuntu D, Lifshay J, Packel L, Batamwita R, Nakayiwa S, et al. Processes and outcomes of HIV serostatus disclosure to sexual partners among people living with HIV in Uganda. AIDS Behav. 2008;12:232-243.
13. Atuyambe LM, Ssegujja E, Ssali S, Tumwine C, Nekesa N, Nannungi A, et al. HIV/AIDS status disclosure increases support, behavioural change and, HIV prevention in the long term: a case for an urban clinic, Kampala, Uganda. BMC Health Serv Res. 2014;14:276.

14. Ebuy H, Yebyo H, Alemayehu M. Level of adherence and predictors of adherence to the Option B+ PMTCT programme in Tigray, northern Ethiopia. Int J Infect Dis. 2015;33:123-129.
15. Ekama SO, Herbertson EC, Addeh EJ, Gab-Okafor CV, Onwujekwe DI, Tayo F, et al. Pattern and determinants of antiretroviral drug adherence among Nigerian pregnant women. J Pregnancy. 2012;2012:851810.
16. Kirsten I, Sewangi J, Kunz A, Dugange F, Ziske J, Jordan-Harder B, et al. Adherence to combination prophylaxis for prevention of mother-to-child-transmission of HIV in Tanzania. PLoS ONE. 2011;6(6):e21020.
17. Kuonza LR, Tshuma CD, Shambira GN, Tshimanga M. Non-adherence to the single dose nevirapine regimen for the prevention of mother-to-child transmission of HIV in Bindura town, Zimbabwe: a cross-sectional analytic study. BMC Public Health. 2010;10:218.
18. Peltzer K, Sikwane E, Majaja M. Factors associated with short-course antiretroviral prophylaxis (dual therapy) adherence for PMTCT in Nkangala district, South Africa. Acta Paediatr. 2011;100:1253-1257.
19. Katz IT, Ryu AE, Onuegbu AG, Psaros C, Weiser SD, Bangsberg DR, et al. Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis. J Int AIDS Soc. 2013;16(Suppl 2):18640.
20. Berg KM, Arnsten JH. Practical and conceptual challenges in measuring antiretroviral adherence. J Acquir Immune Defic Syndr. 2006;43(Suppl 1):S79-S87.
21. Adeniyi OV, Ajayi AI, Selanto-Chairman N, Goon DT, Boon G, Fuentes YO, et al. Demographic, clinical and behavioural determinants of HIV serostatus non-disclosure to sex partners among HIV-infected pregnant women in the Eastern Cape, South Africa. PLoS ONE. 2017;12(8):e0181730.
22. Jasseron C, Mandelbrot L, Dollfus C, Trocmé N, Tubiana R, Teglas JP, et al. Non-disclosure of a pregnant woman's HIV status to her partner is associated with non-optimal prevention of mother-to-child transmission. AIDS Behav. 2013;17:488-497.
23. Koss CA, Natureeba P, Kwarisiima D, Ogena M, Clark TD, Olwoch P, et al. Viral suppression and retention in care up to 5 years after initiation of lifelong ART during pregnancy (Option B+) in rural Uganda. J Acquir Immune Defic Syndr. 2017;74:279-284.
24. Brittain K, Mellins CA, Remien RH, Phillips T, Zerbe A, Abrams EJ, et al. Patterns and predictors of HIV-status disclosure among pregnant women in South Africa: dimensions of disclosure and influence of social and economic circumstances. AIDS Behav. 2018;22:3933-3944.
25. Myer L, Phillips TK, Zerbe A, Ronan A, Hsiao N-Y, Mellins CA, et al. Optimizing antiretroviral therapy (ART) for maternal and child health (MCH): rationale and design of the MCH-ART study. J Acquir Immune Defic Syndr. 2016;72:S189-S196.
26. Myer L, Phillips TK, Zerbe A, Brittain K, Lesosky M, Hsiao N-Y, et al. Integration of postpartum healthcare services for HIV-infected women and their infants in South Africa: a randomised controlled trial. PLoS Med. 2018;15(3):e1002547.
27. Preciago J, Henry H. Linguistic barriers in health education and services. In: Garcia JG, Zea MC, editors. Psychological interventions and research with Latino populations. Boston: Allyn and Bacon; 1997.

28. Brittain K, Mellins CA, Phillips T, Zerbe A, Abrams EJ, Myer L, et al. Social support, stigma and antenatal depression among HIV-infected pregnant women in South Africa. AIDS Behav. 2017;21(1):274-282.
29. Zou G. A modified Poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004;159(7):702-706.
30. Hunter-Adams J, Zerbe A, Philips T, Rini Z, Myer L, Petro G, et al. The dimensionality of disclosure of HIV status amongst post-partum women in Cape Town, South Africa. Afr J AIDS Res. 2017;16(2):101-107.
31. Ramadhani HO, Thielman NM, Landman KZ, Ndosi EM, Gao F, Kirchherr JL, et al. Predictors of incomplete adherence, virologic failure, and antiviral drug resistance among HIV-infected adults receiving antiretroviral therapy in Tanzania. Clin Infect Dis. 2007;45:1492-1498.
32. Ochieng W, Kitawi RC, Nzomo TJ, Mwatelah RS, Kimulwo MJ, Ochieng DJ, et al. Correlates of adherence and treatment failure among Kenyan patients on long-term highly active antiretroviral therapy. J Acquir Immune Defic Syndr. 2015;69:e49-e56.
33. Ostermann J, Pence B, Whetten K, Yao J, Itemba D, Maro V, et al. HIV serostatus disclosure in the treatment cascade: evidence from northern Tanzania. AIDS Care. 2015;27(Suppl 1):59-64.
34. Teshome Yimer Y, Yalew AW. Magnitude and predictors of anti-retroviral treatment (ART) failure in private health facilities in Addis Ababa, Ethiopia. PLoS ONE. 2015;10(5):e0126026.
35. Stinson K, Myer L. Barriers to initiating antiretroviral therapy during pregnancy: a qualitative study of women attending services in Cape Town, South Africa. Afr J AIDS Res. 2012;11(1):65-73.
36. Medley AM, Kennedy CE, Lunyolo S, Sweat MD. Disclosure outcomes, coping strategies, and life changes among women living with HIV in Uganda. Qual Health Res. 2009;19(12):1744-1754.
37. Obermeyer CM, Baijal P, Pegurri E. Facilitating HIV disclosure across diverse settings: a review. Am J Public Health. 2011;101(6):1011-1023.
38. Visser MJ, Neufeld S, de Villiers A, Makin JD, Forsyth BWC. To tell or not to tell: South African women's disclosure of HIV status during pregnancy. AIDS Care. 2008;20(9):1138-1145.
39. Adeniyi OV, Ajayi AI, Goon DT, Owolabi EO, Eboh A, Lambert J. Factors affecting adherence to antiretroviral therapy among pregnant women in the Eastern Cape, South Africa. BMC Infect Dis. 2018;18:175.
40. Spangler SA, Onono M, Bukusi EA, Cohen CR, Turan JM. HIV-positive status disclosure and use of essential PMTCT and maternal health services in rural Kenya. J Acquir Immune Defic Syndr. 2014;67:S235-S242.
41. Hatcher AM, Turan JM, Leslie HH, Kanya LW, Kwena Z, Johnson MO, et al. Predictors of linkage to care following community-based HIV counseling and testing in rural Kenya. AIDS Behav. 2012;16:1295-1307.
42. Varga CA, Sherman GG, Jones SA. HIV-disclosure in the context of vertical transmission: HIV-positive mothers in Johannesburg, South Africa. AIDS Care. 2005;18(8):952-960.
43. Abdool Karim Q, Dellar RC, Bearnot B, Werner L, Frohlich JA, Kharsany ABM, et al. HIV-positive status disclosure in patients in care in rural South Africa:

implications for scaling up treatment and prevention interventions. AIDS Behav. 2015;19:322-329.

44. Makin JD, Forsyth BWC, Visser MJ, Sikkema KJ, Neufeld S, Jeffery B. Factors affecting disclosure in South African HIV-positive pregnant women. AIDS Patient Care STDS. 2008;22(11):907-916.
45. Obiri-Yeboah D, Amoako-Sakyi D, Baidoo I, Adu-Oppong A, Rheinländer T. The 'fears' of disclosing HIV status to sexual partners: a mixed methods study in a counseling setting in Ghana. AIDS Behav. 2016;20:126-136.
46. Patel R, Ratner J, Gore-Felton C, Kadzirange G, Woelk G, Katzenstein D. HIV disclosure patterns, predictors, and psychosocial correlates among HIV positive women in Zimbabwe. AIDS Care. 2012;24(3):358-368.
47. Colombini M, Stöckl H, Watts C, Zimmerman C, Agamasu E, Mayhew SH. Factors affecting adherence to short-course ARV prophylaxis for preventing mother-to-child transmission of HIV in sub-Saharan Africa: a review and lessons for future elimination. AIDS Care. 2014;26(7):914-926.
48. Albrecht S, Semrau K, Kasonde P, Sinkala M, Kankasa C, Vwalika C, et al. Predictors of nonadherence to single-dose nevirapine therapy for the prevention of mother-to-child HIV transmission. J Acquir Immune Defic Syndr. 2006;41(1):114-118.
49. Chaudoir SR, Fisher JD, Simoni JM. Understanding HIV disclosure: a review and application of the Disclosure Processes Model. Soc Sci Med. 2011;72(10):1618-1629.
50. Chaudoir SR, Fisher JD. The Disclosure Processes Model: understanding disclosure decision making and postdisclosure outcomes among people living with a concealable stigmatized identity. Psychol Bull. 2010;136(2):236-256.

Table S7.1 Comparison between women included in analysis of viral load at delivery and women excluded due to insufficient duration on antiretroviral therapy

Variable	Total sample enrolled into follow-up – *n* (%)[1]	Included in analysis	Excluded from analysis	*P*-value
Number of women	628	451	147	
Median [IQR] age	28.0 [24.6, 32.2]	28.4 [24.7, 32.1]	27.6 [24.5, 32.7]	0.885
Educational attainment				
Less than secondary	462 (74)	336 (75)	105 (71)	
Completed secondary/any tertiary	166 (26)	115 (26)	42 (29)	0.462
Currently employed	238 (38)	180 (40)	48 (33)	0.116
Poverty categories				
Most disadvantaged	227 (36)	154 (34)	56 (38)	
Moderate disadvantage	208 (33)	158 (35)	43 (29)	
Least disadvantaged	193 (31)	139 (31)	48 (33)	0.424
Married/cohabiting	259 (41)	192 (43)	55 (37)	0.270
First pregnancy	111 (18)	82 (18)	20 (14)	0.200
Pregnancy intentions				
Unintended	442 (70)	295 (65)	123 (84)	
Intended	186 (30)	156 (35)	24 (16)	<0.001
Median [IQR] gestation in weeks at entry into antenatal care	20 [16, 26]	19 [14, 22]	31 [27, 33]	<0.001
Median [IQR] CD4 cell count	345 [236, 517]	339 [235, 500]	387 [259, 583]	0.091
Timing of diagnosis				
Tested HIV-positive before pregnancy	276 (44)	215 (48)	49 (33)	
Tested HIV-positive during pregnancy	352 (56)	236 (52)	98 (67)	0.002
Disclosed to a male partner by delivery	385 (64)	291 (65)	94 (64)	0.899
Disclosed to ≥1 family/community member by delivery	430 (72)	336 (75)	94 (64)	0.013

[1] Includes 30 women who were lost to follow-up before delivery

Table S7.2 Comparison between women included and excluded from analysis of viral load at 12 months postpartum

Variable	Total sample enrolled into postpartum follow-up – *n* (%)	Included in analysis	Excluded from analysis	*P*-value
Number of women	471	411	60	
Median [IQR] age	27.8 [24.5, 32.3]	28.0 [24.7, 32.6]	26.0 [23.0, 30.5]	0.009
Educational attainment				
Less than secondary	354 (75)	310 (75)	44 (73)	
Completed secondary/any tertiary	117 (25)	101 (25)	16 (27)	0.726
Currently employed	184 (39)	155 (38)	29 (48)	0.115
Poverty categories				
Most disadvantaged	164 (35)	143 (35)	21 (35)	
Moderate disadvantage	158 (34)	137 (33)	21 (35)	
Least disadvantaged	149 (32)	131 (32)	18 (30)	0.950
Married/cohabiting	193 (41)	169 (41)	24 (40)	0.869
First pregnancy	82 (17)	61 (15)	21 (35)	<0.001
Pregnancy intentions				
Unintended	338 (72)	291 (71)	47 (78)	
Intended	133 (28)	120 (29)	13 (22)	0.226
Median [IQR] gestation in weeks at entry into antenatal care	21 [16, 26]	21 [16, 26]	24 [19, 31]	0.016
Median [IQR] CD4 cell count	354 [248, 517]	346 [248, 507]	415 [247, 539]	0.181
Timing of diagnosis				
Tested HIV-positive before pregnancy	198 (42)	183 (45)	15 (25)	
Tested HIV-positive during pregnancy	273 (58)	228 (55)	45 (75)	0.004
Disclosed to a male partner by delivery	292 (62)	258 (63)	34 (57)	0.363
Disclosed to ≥1 family/community member by delivery	332 (70)	295 (72)	37 (62)	0.109
Viral load at delivery				
<50 copies/mL	355 (75)	312 (76)	43 (72)	
≥50 copies/mL	116 (25)	99 (24)	17 (28)	0.476

Chapter 8: Discussion and recommendations

One in three pregnant women in South Africa are living with HIV [1], but pregnant and postpartum women represent a particularly vulnerable group for poor antiretroviral therapy (ART) outcomes. HIV-status disclosure has been widely promoted as beneficial to both population and individual health. At the population level, disclosure may decrease HIV transmission through the adoption of preventive behaviours; at the individual level, disclosure is thought to improve both psychological well-being and adherence to ART. Additional psychosocial factors which may have important implications for adherence include HIV-related stigma and social support, each of which is closely interrelated with disclosure, as well as poor mental health and unintended pregnancy.

This thesis sought to provide insights into the patterns, predictors and impact of HIV-status disclosure among pregnant and postpartum women in the context of lifelong ART in South Africa, including considerations of stigma, social support, depression and unintended pregnancy. This final chapter provides a synopsis of findings in relation to the objectives of this thesis, followed by a discussion of the limitations of this work and then a discussion of key findings. Finally, this chapter presents recommendations for research and practice, including policy guidelines, based on the combined results of this work. Recommendations pertaining to disclosure are aimed at disclosure as both a risk factor and an important outcome in its own right. Additional recommendations are made pertaining to two other major risk factors of interest in this work: HIV-related stigma and unintended pregnancy.

8.1 Synopsis

In Chapter 3, a novel analytic technique was used to describe patterns of disclosure during pregnancy and postpartum. Based on the findings from this analysis, disclosure was assessed as two separate dimensions in subsequent chapters: disclosure to a male partner, and disclosure to family/community members. As well as describing patterns of disclosure, this chapter examined predictors of disclosure to male partners and to family/community members to address the first objective of this thesis. This chapter highlighted that social and economic circumstances are central determinants of disclosure. Chapter 4 addressed the second objective of this thesis by exploring associations among stigma, social support and depression during pregnancy. This chapter highlighted the profound negative impact of stigma: in this sample, stigma modified the association between social support and depressive symptoms such that higher levels of social support were not associated with lower levels of depression among women reporting high levels of stigma.

Key assumptions related to disclosure which this thesis sought to test included: (i) that disclosure is universally beneficial with (ii) effects that are consistent over time, and (iii) that these benefits are consistent across the person(s) to whom individuals disclose. Chapter 5 tested these assumptions as part of an exploration of the impact of disclosure on depressive symptoms during pregnancy and postpartum, as well as the role of pregnancy intention in this relationship. The findings presented in this chapter suggest that unintended pregnancy modifies the impact of disclosure to a male partner on depressive symptoms during pregnancy among women who had been newly diagnosed HIV-positive during their pregnancy. In this group of women, disclosure to a male partner was associated with lower levels of depression among women who reported that their current pregnancy was intended but was associated with higher levels of depression among women who reported that their

pregnancy was unintended. Chapter 5 additionally showed that the effects of disclosure on depression are neither consistent over time nor consistent across the person(s) to whom women disclose. Chapter 6 addressed the fourth objective of this thesis by exploring the impact of unintended pregnancy on viral load during the postpartum period. This chapter presented novel evidence that unintended pregnancy is a prevalent and persistent predictor of elevated viral load up to five years postpartum.

Finally, Chapter 7 addressed the fifth objective of this thesis and, along with Chapter 5, tested the three assumptions that this thesis aimed to critique. This chapter provided strong evidence against these assumptions and suggested that the association between disclosure and viral load is complex. The findings presented in this chapter suggest that the association between disclosure and viral load is modified by three factors: (i) timing of HIV diagnosis (before versus during pregnancy); (ii) relationship to the person(s) to whom women disclose, and (iii) in the case of disclosure to a male partner, relationship status.

8.2 Strengths and limitations

Limitations pertaining to each analysis were included in each of the results chapters, but there are overarching limitations that must be considered prior to discussing the key findings of this body of work and making recommendations.

First and foremost, these data arise from a single population: pregnant and postpartum women. Levels of disclosure to partner(s) are significantly lower among women compared to men [2-5], and disclosure to male partners may be particularly difficult among women tested in the context of antenatal care [6], as discussed in Chapter 2. Women test for HIV at much higher rates than men and face a disproportionately higher obligation to disclose [7, 8], but

unstable relationships and high levels of migrant work in countries such as South Africa may contribute to difficulties related to disclosing to male partners [7, 9, 10]. Coupled with this, women's economic dependence on their partners may make them particularly vulnerable and may decrease the odds of disclosure [8, 11-16]. Among women initiating ART during pregnancy in the study from which these data arise, just over half of women were diagnosed HIV-positive during their current pregnancy; one-quarter had completed secondary education; and only two in five were employed (Chapter 4). The vulnerability of this particular sample may have profound implications for the patterns and predictors of disclosure observed here, and these findings should be extrapolated to other pregnant and postpartum populations with caution. As more women enter antenatal care already on ART, due to the adoption of Option B+ guidelines, the results observed here may change in important ways. Finally, it has been acknowledged throughout that the findings and discussion thereof should be extrapolated to non-pregnant populations with caution.

A further issue related to generalisability is that these data arise from a single site, the Gugulethu Midwife Obstetric Unit (MOU) in Cape Town, South Africa. The impact that context may have on the findings presented in this thesis was discussed in Chapter 2, but key impacts are repeated here. All of the constructs explored in this thesis are situated within a broader social, cultural and political context [17]. Levels of stigma remain high in the country [18-20], despite increased ART availability and uptake. As represented in the conceptual frameworks presented in Chapter 2, stigma is a critical construct in relation to disclosure, adherence and mental health, and the findings from this thesis may be profoundly different in contexts with different levels of stigma. Again, the findings presented herein should be extrapolated to other settings with caution.

There are limitations to determining causality of the results arising from this research. As discussed in Chapter 2, disclosure may result directly in improved adherence and consequent viral suppression or may be a marker of factors such as more supportive relationships [21-23]. The causality of observed associations between pregnancy intentions and improved outcomes is similarly difficult to determine, given that pregnancy intentions are influenced by interrelated factors at the individual, couple, family and community levels [24]. The data presented herein arise from an observational study, and the potential for residual and unmeasured confounding cannot be ignored. However, many of the exposures of interest in this thesis, for example disclosure, stigma and unintended pregnancy, are not amenable to randomisation. As such, no other study design could have provided stronger evidence for the associations observed. In all analyses, potential confounders were included in models of the exposure-outcome association. Given that the data included were constrained by what factors were measured in the study from which these data arise, and the schedule of measurements, an exploration of mechanisms was not possible. Issues related to causality and mechanisms are discussed further below as critical caveats to the findings from this work.

As stated above, the data presented herein were constrained by the measurements undertaken in the study from which these arise. Disclosure was assessed using self-report, and only voluntary disclosure was assessed. It has been shown that self-reported disclosure is not necessarily concordant with confirmation of the disclosure act by the person(s) to whom individuals report having disclosed [25]. Only pregnant women were enrolled into this study and confirmation of disclosure was not assessed. Although this is a limitation of this work, confirming disclosure would be very resource intensive and, as such, may not be feasible in research and practice. Women were asked to report whether or not they had disclosed to each person in a list of persons. Allowing women to report to whom they had disclosed without the

use of a list of possible persons may have resulted in different responses. However, the use of a list may have prompted women to report having disclosed to particular individuals who they may not have reported if disclosure was assessed as an open-ended question.

Three further important limitations related to the way in which disclosure was assessed and treated in analyses are: (i) only voluntary acts of disclosure were assessed, and involuntary disclosure may lead to negative responses and, consequently, poorer outcomes; (ii) responses to disclosure were not assessed and, as argued in various parts of this thesis, these responses may be critical determinants of whether or not disclosure is beneficial; and (iii) the response options 'No' and 'Not applicable' regarding disclosure to each possible person were combined in analyses. This third limitation meant that women who had decided not to disclose to a particular person and women who had not disclosed because this person is not present in their life were combined in one group in analyses, which may conflate disclosure events with the size of an individual's social network. Given that the intention was to compare women who had disclosed to women who had not disclosed, regardless of reason, this approach was appropriate, but more nuanced analyses where these categories are separated may lead to different results.

A further limitation related to measurement is the way in which stigma was assessed. In the broader study, a subset of items from the Social Impact Scale, which was developed in the United States, was used to measure stigma, and other scales may have been more valid in this population of South African pregnant women. Further, only enacted stigma (in the form of social rejection) and internalised stigma were assessed, thus these results do not speak to the potential impact of perceived and anticipated stigma. In addition, intersectional stigmas, for

example stigma related to socioeconomic status or unintended pregnancy, and structural stigma were not assessed [26].

Differences in the measures included in analyses and analytic methods used arose over time as this work progressed, and some analyses used more robust measures than others. For example, some analyses used the single measure of unintended pregnancy while others used the more sophisticated London Measure of Unplanned Pregnancy (LMUP). As stated in Chapter 1, these two measures have been compared within this cohort with high levels of concordance [27], thus the conclusions are likely robust despite the different measures used.

This thesis explored the impact of disclosure on two outcomes: depressive symptoms and HIV viral load. Disclosure may have other benefits, and the findings presented herein may not be generalisable to other outcomes. In addition, intimate partner violence may be critically related to disclosure to sexual partners, but an in-depth exploration of intimate partner violence was beyond the scope of this thesis. Finally, missing data is an important limitation of this work, both by design, as only breastfeeding women were followed during the postpartum period, and by missed study visits. However, sensitivity analyses were conducted as part of many of these analyses to explore the impact of missing data.

Despite these limitations, this thesis notably extends the literature in several areas. These analyses are strengthened by the consideration of subgroups; inclusion of prospectively-collected data; and use of nuanced disclosure measures which allowed an exploration of disclosure to different persons. Alongside the nuanced measures of disclosure, these analyses used a novel method to explore the patterns of disclosure that informed subsequent analyses. In addition, the analyses presented in Chapter 6 used a robust and well-validated measure of

unintended pregnancy: the LMUP. Viral load, a robust biological and clinical outcome, was included as an outcome in these analyses. Further extensions to the literature include the exploration of interrelationships between constructs of interest, including stigma, social support and depression; an investigation of the effects of disclosure on depression, for which the evidence is mixed; and a consideration of the long-term effects of unintended pregnancy, an understudied issue. Each of these contributions to the literature is expanded on in the discussion below.

8.3 Discussion of key findings

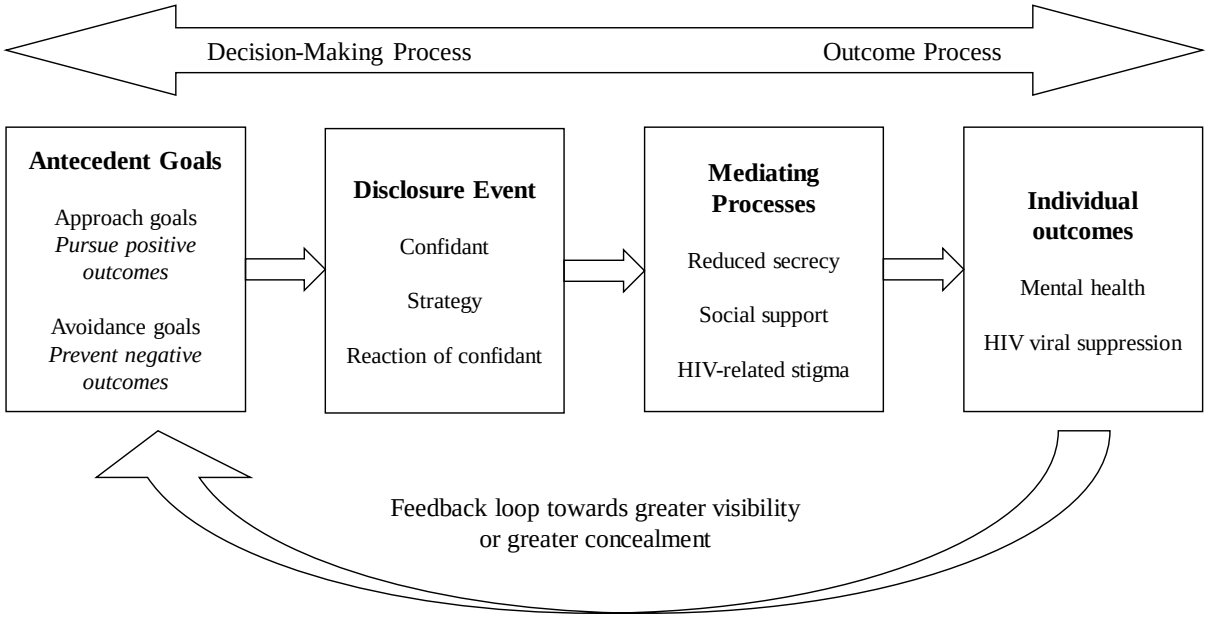
While keeping in mind the limitations described above, this section presents a discussion of key findings prior to making recommendations. This discussion focusses on three broad underlying themes: (i) the individual is central to disclosure; (ii) disclosure occurs within social relationships; and (iii) pregnancy is a critical window.

8.3.1 The individual is central to disclosure

Over a decade ago, Remien and Mellins [28] argued that we cannot forget the individual in our global response to the HIV pandemic. Public health approaches are centred on population-level interventions to improve health and well-being and are typically not tailored to the individual. However, the findings of this work strongly suggest that the individual is central to our understanding of disclosure. In particular, women's social and economic circumstances appear to be central determinants of disclosure, as demonstrated in Chapter 3; and the beneficial effects of disclosure on depression and viral load appear to be contextual rather than universal, as demonstrated in Chapters 5 and 7. Taken together, these findings suggest that individual women's characteristics may critically determine whether or not they disclose as well as whether or not disclosure is beneficial. Further, the findings reported in

Chapter 4 suggest that women's experiences of stigma determine whether or not their perceived level of social support buffers against depression during pregnancy. It is worthwhile to revisit Figure 2.1 as a useful conceptual understanding of disclosure [29, 30] on which this thesis draws, and to frame the remainder of this section of the Discussion.

Re-presentation of Figure 2.1. Disclosure Processes Model, adapted for this thesis [29, 30]



Individuals have different antecedent goals related to disclosure, represented as approach and avoidance goals in the figure above. Indeed, Chapter 2 reported that women's motivations for disclosing to, for example, family members differ from their motivations for disclosing to a male partner [31, 32]. Although most individuals disclose to at least one person [33], strategies for disclosure range from widespread to selective disclosure [34]. In addition, individuals disclose in different ways, and not always directly [32, 35, 36]. These differences are represented as part of the disclosure event in the figure above. Despite widespread acceptance that individuals have vastly different disclosure experiences, however, the

predominant narrative in each of research, practice and policy is that disclosure is universally beneficial, i.e. that the benefits of disclosure do not differ across individuals.

Indeed, disclosure is framed in each of research, policy and practice as an act that should be strongly, and universally, encouraged. Authors have stated, for example, that it is 'commonly accepted' that disclosure leads to higher levels of psychosocial support and ART adherence, ultimately improving treatment outcomes and reducing the risk of HIV transmission [37]; or that their findings that non-disclosure is associated with suboptimal adherence are 'predictable' [38]. Disclosure has even been described as critical to HIV prevention, through increased support for preventive actions, easier access to HIV services and the prevention of sexual transmission [39], with others arguing that reductions in HIV incidence as well as in stigma and discrimination will not be achieved without disclosure [17]. Authors have even gone as far as to state that healthcare providers and policymakers need to convince people to disclose their HIV status in cases where they are reluctant to do so [40-42].

Numerous quantitative studies have demonstrated associations between disclosure and improved adherence to ART among pregnant women [43], but few have considered the possibility that the benefits of disclosure may differ in different subgroups and that disclosure may not be universally beneficial. A notable exception is an early study that reported that disclosure to a male partner was only associated with adherence to single-dose nevirapine (NVP) among women who delivered at home [44]. It has been previously noted that context and individuals' living environments moderate both the patterns of disclosure and its consequences [45]. The findings presented in this thesis are along these same lines, and notably extend the literature by providing strong evidence against the assumption that disclosure is a universally beneficial act. Indeed, the findings from Chapter 5 suggest that

disclosing to a male partner may lead to higher levels of depressive symptoms among newly-diagnosed women who experience an unintended pregnancy. It has been argued that disclosure may not always be in the best interests of women [46], and this thesis demonstrates that disclosure may in fact be harmful in this group of women. Other authors have argued that disclosure is not a universally positive act [34] and that disclosure does not have one inevitable outcome [17]; this thesis provides strong support for these viewpoints.

Although the data on which this thesis draws preclude an exploration of mechanisms and causality, as noted in the limitations section above, several hypotheses can be considered. First, and drawing on the conceptual framework above, the reaction of the person(s) to whom women disclose may be critical determinants of whether or not disclosure is beneficial [47]. Disclosure may lead to increased social support or increased stigma, and these outcomes may similarly be critical in terms of whether or not the disclosure act is beneficial [48]. This thesis demonstrated that when levels of stigma are high, social support does not buffer against depression; where levels of stigma are high, it is plausible that lower levels of disclosure are in fact protective [49]. A further hypothesis is that disclosure is a marker of a more supportive relationship. Indeed, individuals are more likely to disclose to individuals who they deem to be supportive [50], and non-disclosure may be a marker of an unhealthy relationship [46]. The findings presented in this thesis suggest that disclosure to a male partner is beneficial among women who are married and/or cohabiting. The importance of relationships is discussed further under Section 8.3.2, below, but it is plausible that whether or not disclosure is beneficial is determined by the responses of the individual(s) to whom women disclose, and the quality of their relationships with these individual(s).

A further hypothesis to consider is that there is a critical window during which disclosure is most beneficial. The findings presented herein suggest that the benefits of disclosure are not consistent over time but rather that disclosure is particularly beneficial during pregnancy among women who were newly diagnosed HIV-positive during the pregnancy. As disclosure did not appear to have beneficial effects on viral load among women who were diagnosed prior to the pregnancy, it is plausible that it is the timing of diagnosis that is critical, and that among newly-diagnosed women this critical window coincides with pregnancy. The importance of this window is discussed further under Section 8.3.3, below. Finally, this thesis highlighted that unintended pregnancy is both a moderator of the relationship between disclosure to a male partner and depression as well as a persistent predictor of poor ART outcomes. This is in line with the hypothesis that context moderates both the patterns of disclosure and its consequences [45]. Indeed, Chapter 3 demonstrated that the intendedness of the pregnancy is an important predictor of disclosure to a male partner.

Taken together, this thesis presents compelling evidence that disclosure is not universally beneficial and that the individual is central to our understandings of disclosure, although it cannot definitively explain why disclosure appears to be beneficial in some women but not among others.

8.3.2 Disclosure occurs within social relationships

The findings presented in this thesis highlight the relational aspects of disclosure. Disclosure is inherently an act that occurs within social relationships [50]. Indeed, the socio-ecological framework [51], which is described in Chapter 2 and on which this thesis draws, situates disclosure within the level of family and peer influences on adherence. It has been suggested that whether or not an individual discloses to a particular person is an indicator of social

connectedness and the quality of the relationship [52]. As discussed in Chapter 2, the majority of disclosure research to date has operationalised disclosure as any versus no disclosure and has not provided a rationale for how disclosure was assessed and/or treated in analysis. Using a novel methodological approach, Chapter 3 describes how disclosure forms two separate dimensions in the sample of women from which these data arise. Further, this chapter demonstrates that the determinants of these two forms of disclosure differ; this finding would not have been observed if disclosure had been treated in analysis as a binary variable indicating any versus no disclosure. As alluded to above, motivations for disclosing to different individuals may differ; these quantitative data suggest that different individual characteristics may determine the likelihood of disclosure to different people.

As discussed above, the quality of relationships may critically determine the outcomes, both positive and negative, of disclosure. However, there are few explicit considerations of whether disclosure to different individuals has different effects. As highlighted in Chapter 2, it is unclear whether researchers have explored outcomes across different dimensions of disclosure and have only reported significant associations, or whether they did not consider that effects may differ according to the person(s) to whom individuals disclose. A notable exception is a study from Kenya which suggested that self-reported adherence was associated with disclosure to (i) anyone, (ii) a male partner and (iii) an immediate family member, but not with disclosure to others, including friends, more distant relatives and members of the community [48]. The third assumption which this thesis aimed to test was that the benefits of disclosure are consistent across the person(s) to whom individuals disclose, such that the benefits of disclosing to, for example, a male partner are consistent with the benefits of disclosing to a sister or friend.

Chapter 5 demonstrated that disclosure to a male partner is associated with depressive symptoms during pregnancy, but that disclosure to family/community members was associated with depressive symptoms during the early postpartum period. In line with this, Chapter 7 demonstrated that disclosure to a male partner is associated with viral load at delivery among women who are newly-diagnosed HIV-positive and in a married and/or cohabiting relationship; and that disclosure to family/community members is associated with viral load at 12 months postpartum among newly-diagnosed women. Taken together, these findings suggest that the person(s) to whom women disclose is important, and that the potential benefits of disclosure for depressive symptoms and viral load outcomes are not consistent across these person(s). In addition, the finding that disclosure to a male partner is more likely among women who are married and/or cohabiting (Chapter 3) and is only associated with viral load at delivery among newly-diagnosed women who are in a married and/or cohabiting relationship (Chapter 7) lends further support to the argument that relationship quality critically determines both the likelihood and the benefits of disclosure.

Along with disclosure occurring within social relationships, an HIV diagnosis and consequent decisions about whether or not to disclose occur in the context of pre-existing psychosocial and economic stressors [53]. As summarised in the review of the literature in Chapter 2 and alluded to above, disclosure to a male partner is particularly challenging in contexts where women are socially and economically dependent on their partner. Chapter 3 shows that higher levels of poverty are associated with a reduced likelihood of disclosure to a male partner among women who are neither married nor cohabiting, speaking to women's economic vulnerability [54]. A further psychosocial stressor that plays a central role in several parts of this thesis is unintended pregnancy, with the findings suggesting that unintended pregnancy is

a critical stressor in the context of prevention of mother-to-child transmission (PMTCT). Findings related to pregnancy intention are discussed further in Section 8.3.3, below.

A final construct related to social relationships that warrants discussion is that of HIV-related stigma. The socio-ecological framework presented in Chapter 2 situates stigma within the level of community determinants of adherence [51] but acts of stigma also occur within social relationships [26]. Drawing on the Disclosure Processes Model re-presented above [29, 30], the goal of avoiding stigma may reduce the likelihood of disclosing, but social rejection following disclosure may also lead to poorer outcomes; indeed, non-disclosure has been described as a manifestation of stigma [26]. Stigma has also been identified as a determinant of social support [55], mental health [56] and, ultimately, treatment outcomes [57]. In line with this, Chapter 4 extends the literature by highlighting the interrelationships among stigma, social support and depression among women initiating ART during pregnancy. In this sample of women, both social rejection and internalised shame were found to be strongly associated with depressive symptoms, although stronger effects were observed for internalised shame. Further, this chapter demonstrated that higher levels of social support do not buffer against the detrimental effects of stigma on depression in this sample. These findings speak to the profound negative effects of stigma in this population. Despite the hope that levels of stigma would decrease over time as more people initiated ART, stigma remains a pervasive and harmful issue [18-20].

As highlighted in this section, this thesis provides quantitative evidence that social relationships are key to understanding disclosure: the patterns and determinants of disclosure to different individuals differ; the quality and nature of women's relationships with their

partners are profound determinants of disclosure and the benefits thereof; and stigma remains a pervasive and harmful factor at the social and community level.

8.3.3 Pregnancy is a critical window

A key assumption that this thesis sought to test was that the effects of disclosure are consistent over time. Despite being viewed as a sequential process that occurs over time [17, 35], much of the existing literature has relied on cross-sectional data to investigate each of the patterns, determinants, and effects of disclosure. Chapter 2 provided an overview and critique of existing studies, including the finding that significant effects of disclosure on adherence are more frequently reported in cross-sectional compared to longitudinal studies [58]. This thesis notably extends the literature by including both cross-sectional and prospectively-collected data. Chapter 5 provides evidence that disclosure to each of a male partner and to family/community members are associated with depressive symptoms at some time points but not at others. Similarly, the findings from Chapter 7 suggest that disclosure to a male partner is associated with a reduced risk of elevated viral load at delivery among women who tested HIV-positive during the pregnancy; and that disclosure to family/community members is associated with a reduced risk of elevated viral load at 12 months postpartum in this same group of women. In contrast, disclosure was not associated with viral load at entry into antenatal care among women who were diagnosed before the pregnancy and were established on ART, or at delivery or 12 months postpartum among women who were diagnosed before the pregnancy and were initiating ART.

These results suggest that the effects of disclosure on each of depressive symptoms and viral load are not consistent over time. Rather, it appears as though there may be a critical window during which disclosure affects depressive symptoms and viral load among newly-diagnosed

women and, as stated above, this critical window coincides with pregnancy. Newly-diagnosed women need time to come to terms with their diagnosis [6] and to establish adherence behaviours, and disclosure may be beneficial for some women during this period. Over time, however, disclosure does not appear to be a primary driver of depressive symptoms or viral load outcomes in this population. Pregnancy has previously been described as a 'teachable moment', defined as an event or experience which presents an opportunity for learning [59]. This window may be particularly amenable to interventions based on mothers' desires for a healthy pregnancy and baby and their adoption of a new social role [59, 60]. In South Africa, is has been previously noted that women prioritise antenatal and HIV care for the health of their baby but are less motivated to seek care for their own health during the postpartum period [61]. The data presented in Chapter 6 suggest that viraemia increases with increasing time postpartum, suggesting that the motivation to maintain high levels of adherence may decrease over time. As stated in the limitations section above, these findings should be extrapolated to non-pregnant populations with caution, and it remains unclear whether disclosure in the period of time immediately post-diagnosis may similarly improve outcomes outside of the context of pregnancy.

A further critical finding related to pregnancy is the importance of the intendedness of the pregnancy. As argued in various parts of this thesis, unintended pregnancy has long been acknowledged as a prevalent issue [62, 63] which heightens women's vulnerability [54, 64, 65]. However, there is limited quantitative evidence for the impact of unintended pregnancy on women's health and well-being, particularly in the context of HIV. Chapter 3 demonstrates that an unintended pregnancy reduces the likelihood of disclosure to a male partner among women diagnosed HIV-positive during the pregnancy, and Chapter 5 describes unintended pregnancy as a modifier of the association between disclosure to a male

partner and depressive symptoms in this group. Chapter 6 then presents compelling evidence for the long-term negative impact of an unintended pregnancy, demonstrating associations with elevated viral load up to five years after delivery.

As highlighted in this section, the findings from this thesis suggest that pregnancy is a critical window during which disclosure may improve ART outcomes, but that the intendedness of the pregnancy is critical in terms of affecting disclosure; heightening women's vulnerability; and determining long-term HIV treatment outcomes.

8.4 Recommendations for research

The discussion above leads to several recommendations for research. Although alluded to in various parts of this thesis, they are summarised here in order to provide overarching recommendations. Following this, additional recommendations are made relating to methodological aspects of research.

8.4.1 Disclosure research

Disclosure has long been acknowledged as an important issue in the lives of HIV-infected individuals [28]. As such, there has been much research interest in the act of disclosure, and it is likely that this research focus will continue. However, if it can be accepted that disclosure may not be universally beneficial, then the focus of research should shift to a focus on when and why disclosure is likely to be beneficial [30]. This necessitates explorations of sub-groups: context and individual's social and economic circumstances must be taken into account when exploring the determinants and impacts of disclosure. Pertinent sub-groups arising from this research include women who are married and/or cohabiting versus those who are neither married nor cohabiting; women who are experiencing an unintended versus

intended pregnancy; and women who were newly-diagnosed during their current pregnancy versus those diagnosed before the pregnancy. Other sub-groups may be more relevant among non-pregnant adult populations, and these should be explored in future research.

A second recommendation for future research is that longitudinal data are critical in exploring patterns and the impacts of disclosure. This thesis showed that the effects of disclosure on depressive symptoms and viral load are not consistent over time; these results would not have been observed using only cross-sectional data. Further, the findings from this thesis suggest that the benefits of disclosure are not consistent across the person(s) to whom women disclose. It is recommended that researchers first explore the dimensionality of disclosure in their samples before operationalising disclosure, as has been argued previously [66, 67]. Without this exploration, both the differing determinants of disclosure and the differing impacts of disclosure to different person(s) may be lost in analysis. Although not measured in the study from which these data arise, individuals' responses to disclosure should be explored in future research as important determinants of the impact of disclosure, in line with the Disclosure Processes Model.

8.4.2 Stigma research

As discussed in Chapter 2, the negative effects of HIV-related stigma on mental health and on treatment outcomes have been definitively established, but there are nuances that have been less frequently explored that should be addressed in future research. In particular, there have been few considerations of the impacts of different types of HIV-related stigma on health and HIV treatment outcomes [26]; future research should explore these as well as the impacts of structural and intersectional stigmas. As structural stigma by definition will differ across contexts, and intersectional stigma and forms of HIV-related stigma may similarly differ

across context, research which includes multiple communities would be beneficial in order to explore findings across settings. A critical research need in the field of HIV-related stigma is an exploration of mediators and moderators. Methodological considerations are discussed under Section 8.4.4, below, but it should be noted here that investigations of the mechanisms that lead to poor mental health and treatment outcomes, as well as factors that may protect against these outcomes, are needed in order to inform intervention efforts.

8.4.3 Unintended pregnancy research

This thesis provides novel evidence for the long-term impacts of an unintended pregnancy on elevated viral load during the postpartum period. As argued in Chapter 6, unintended pregnancy should be escalated as a global public health concern. Alongside this recommendation, the findings from this thesis suggest that unintended pregnancy warrants further attention in quantitative research. Much qualitative work has highlighted the heightened vulnerability that women face in the context of an unintended pregnancy, as discussed in various parts of this thesis, but additional research is needed to (i) explore the long-term impacts of an unintended pregnancy on maternal and child health and (ii) examine the role of unintended pregnancy as a potential effect modifier in other associations regarding psychosocial well-being during pregnancy. Finally, the methodological limitations of assessing unintended pregnancy were discussed in Chapter 6, and future research should focus on how best to measure this construct as well as changes in pregnancy intentions and desirability from the pre-conception period through delivery; this latter recommendation will require longitudinal data.

8.4.4 Methodological considerations

Methodological recommendations are made throughout this work and in the sections above but are summarised and expanded on here. First, the three assumptions which this thesis sought to test lead to three critical recommendations: (i) sub-groups must be considered when exploring the patterns and impacts of disclosure, given the findings related to effect modification presented in this thesis; (ii) longitudinal data are needed to parse out changes in the effects of disclosure over time; and (iii) disclosure must be operationalised with considerations of the different person(s) to whom individuals disclose. Effect modification was evident in most chapters of this thesis. Chapter 3 showed that the determinants of disclosure to a male partner differ across relationship status; Chapters 5 and 7 showed that the impacts of disclosure differ across pregnancy intentions and across timing of diagnosis and relationship status, respectively. In line with this, Chapter 4 showed that the impact of social support on depressive symptoms is modified by stigma. Taken together, these findings suggest that sub-groups are central to our understandings of these constructs and should be considered in all future research. Second, longitudinal data are necessary to explore patterns and outcomes of disclosure over time, given that disclosure is a process, and to explore dynamic relationships between psychosocial constructs as well as the long-term impacts of these constructs over time. The importance of exploring the dimensionality of data is argued above, and researchers should use comprehensive measures of disclosure to allow for this exploration of dimensionality. The importance of future studies focussing on the measurement of unintended pregnancy is noted above.

The findings presented in this thesis and the limitations thereof lead to several recommendations relating to analytic methods and causal thinking. Clearly, recommendations made above regarding sub-groups, longitudinal data and the operationalisation of disclosure

have analytic implications. In addition, both the design and analysis of future research should be strongly informed by causal considerations. The constructs of interest in this thesis are critically interrelated, as is evident from the preceding chapters, and arise within complex social contexts and relationships. As such, causality is difficult to determine. Future research must consider potential confounders and should be driven by and empirically test existing causal frameworks pertaining to these constructs. In particular, it was noted in various parts of this thesis that these data did not allow for an exploration of the mechanisms of the associations observed. Causal frameworks are critical to future explorations of these mechanisms, and the importance of elucidating these is discussed under Section 8.5.7, below. Finally, it is critical to re-emphasise that all of these findings arise from a cohort of pregnant women in South Africa. The implications of context were discussed in Chapter 2, but it must be reiterated that these findings should be extrapolated to non-pregnant populations and other settings with caution. Future research should investigate the similarities and differences of these findings when similar research is conducted in other populations and settings.

8.5 Recommendations for practice

In addition to recommendations for research, several recommendations for practice and policy arise from this work. At the outset, it is important to note that social context strongly shapes patterns of disclosure [67]. Disclosure patterns may be expected to differ widely in contexts where, for example, non-disclosure is criminalised, women are heavily dependent on their male partners, or levels of HIV-related stigma are high. The data on which this thesis are based arise from a single community in South Africa. The influence that context might have on the findings presented here was discussed in Chapter 2, but it is important to note that recommendations given here are tailored to the context of pregnancy in South Africa and should be generalised to other settings with caution. Recommendations are made regarding

existing practices, for example better implementation of existing guidelines, as well as regarding the potential for interventions to improve outcomes. The potential interventions discussed here are specifically targeted toward HIV-infected pregnant and postpartum women and may not be appropriate or effective in populations of non-pregnant adults.

8.5.1 Individualised counselling

This discussion of key findings began by noting that public health approaches are centred on population-level interventions and are typically not tailored to the individual. However, this thesis presents strong evidence that the individual is central. Disclosure is ultimately a personal matter [28], and the individual cannot be ignored in counselling. Indeed, an early article argued that blanket disclosure in all circumstances should not be advised [22], and others have argued that it is not possible to develop a generic template for disclosure counselling that would be helpful for all HIV-infected people [34]. This thesis provides strong support for these arguments, with Chapter 3 concluding by stating that counselling messaging should ideally be tailored to the broader social and economic circumstances of individual women's lives. Chapter 7 notes that individualised counselling may not be feasible in busy primary care settings, but this section recommends that individualised counselling at least be provided for particular sub-groups.

A particularly vulnerable sub-group who may benefit most from individualised counselling is women who are newly diagnosed HIV-positive in the context of an unintended pregnancy. Pregnancy is a socially vulnerable period [36], but there is ample qualitative evidence, summarised in the literature review presented in Chapter 2, that an unintended pregnancy confers additional vulnerability, with this thesis providing quantitative evidence that this vulnerability continues into the postpartum period. It has been argued that it is reasonable to

delay counselling messaging that emphasises immediate disclosure among women experiencing a new HIV diagnosis in the context of an unintended pregnancy, in order to support women to come to terms with their diagnosis before they are able to disclose [54]. Based on the findings presented in this thesis, counselling messaging among this group of women should focus not only on disclosure, but also on the potential adverse impacts of the unintended pregnancy.

Given that women repeatedly visit antenatal clinics during pregnancy, the antenatal period represents a window of opportunity during which well-trained healthcare providers and lay counsellors could support women who are most vulnerable. Ongoing supportive counselling should be offered during this period, not limited to the time of diagnosis [6]. Postpartum women in South Africa report that responses to disclosure range from supportive to angry and disappointed [32], and some women experience negative outcomes such as abandonment and violence [6, 15]. Counselling services need to be made available for women who experience negative outcomes after disclosing.

8.5.2 Non-disclosure as an appropriate response

In line with the argument about negative reactions above, it is recommended that non-disclosure be recognised as an appropriate response in certain situations. From a public health perspective, the encouragement of all HIV-infected individuals to disclose their HIV status to their sexual partner(s) has been described as ‘sound in its intention’ [53]; this thesis makes the argument that disclosure may not always be beneficial and may in fact be harmful in some situations. An example is contexts in which levels of stigma remain high: in these settings, non-disclosure may be an appropriate alternative to revealing one’s HIV-positive status given the potential for experiencing enacted stigma. Among HIV-infected women in

India, for example, concealing one's HIV status has been described as essential in order to avoid stigma and maintain a normal life [49]. Disclosure is universally promoted in policy and in counselling services, but the environment in which HIV-infected individuals live may not always encourage or be conducive to disclosure.

Non-disclosure should also be viewed as appropriate in situations in which abuse is a possible response to disclosure [68]; in these situations, non-disclosure may be a reasoned response to a dangerous situation [69]. Notably, intimate partner violence is prevalent in South Africa [70] but considerations of violence are absent from recommendations promoting blanket disclosure in all circumstances. Further, the evidence base for interventions to facilitate safer disclosure among women who fear or are experiencing violence is limited [71]. Support for disclosure must protect women's rights, autonomy and safety [48], drawing on the principle of doing no harm [46], and counsellors should be made aware that there will always be women for whom disclosure is not a safe or recommended behaviour [72].

Healthcare providers and lay counsellors should ideally be trained not only to recognise that disclosure may not always be in a woman's best interests, but also to discuss partner dynamics [69]. Currently, counselling about disclosure does not include discussions of strategies to address the very relationship characteristics that may make women reluctant to disclose [73]; indeed, counselling about disclosure should ignore neither the individual nor the couple. It has been previously argued that counselling to enhance trust and a supportive relationship may facilitate disclosure within couples [74]. However, counselling messaging must take into account that in settings such as South Africa, stable relationships characterised by trust and support may not be the norm, as highlighted in the review of the literature presented in Chapter 2.

Early guidelines for the management of HIV in pregnant women stated that all women should be encouraged to disclose to their partner [75]. Over time, it has been recognised that not all women are able to or want to disclose. For healthcare workers and counsellors, this creates an ethical dilemma of balancing the desire to prevent HIV transmission with that of providing support to HIV-infected women and respecting their privacy [76]. A discussion of the ethics of disclosure is beyond the scope of this thesis. Drawing on the findings of this thesis, however, the recommendations for practice and policy presented here centre on promoting disclosure as an act that may be beneficial for some women and in some circumstances, rather than as a universally beneficial act. It is recommended that counselling messaging allows for the possibility that women's individual characteristics and the quality of their relationships critically shape disclosure and its benefits. As disclosure occurs as a process of revealing one's status to an increasing number of individuals over time, disclosure decisions have to be made repeatedly [33], and evidence suggests that disclosure does not become easier over time [77]. As such, ongoing supportive counselling may be needed.

8.5.4 Facilitating disclosure

While recognising that non-disclosure may be an appropriate response in some situations, disclosure may benefit some individuals and lead to population-level benefits and should be supported where appropriate. In low- and middle-income countries (LMICs), interventions to increase disclosure have included cognitive-behavioural support groups; using peers or community health workers to provide individual support for disclosure; or using partner notification by healthcare providers, with mixed results [78]. Similarly, a recent systematic review including five intervention studies which sought to increase disclosure to sexual partners in the United States reported mixed success [72].

In South Africa and many other settings, women face a disproportionately high burden of disclosure, as discussed earlier in this thesis. Recognising this, it has been suggested that facilitated disclosure, where a healthcare worker acts as an intermediary, may benefit pregnant women [79, 80]. However, it has also been argued that using women as a go-between to increase male partner testing may add an unnecessary burden on women [81], and no single method of facilitated disclosure will be appropriate for every pregnant woman [80]. Ultimately, shifting the burden of disclosure away from women is critical. A further suggestion to increase disclosure is to promote couples counselling and testing [79, 80], although the uptake of this approach remains extremely low [82]. Finally, home-based testing may improve the yield of testing and mutual disclosure [81].

In addition, the purpose of an intervention to increase disclosure should be carefully considered. For example, partner notification to warn of possible exposure and encourage the adoption of preventive behaviours and disclosure to increase support for the HIV-infected individual are two different goals. It has been noted that contextual factors are critical in thinking about adherence interventions, as the effectiveness of interventions may differ across settings [83]. If facilitating disclosure is thought of as an intervention to improve adherence, then context must be considered; indeed, the importance of context has been alluded to throughout this thesis. In contexts where levels of stigma are particularly high, for example, interventions to increase disclosure may be less effective. In addition, timing must be considered: facilitating disclosure may be most helpful during pregnancy among newly-diagnosed women, which may reduce the risk of mother-to-child transmission (MTCT), but disclosure interventions at other timepoints may be less beneficial. In line with the discussion of individualised counselling, above, interventions targeted at those who may benefit most from disclosure should be considered. However, given that disclosure may not always benefit

HIV-infected individuals and may lead to harm in certain situations, the purpose of interventions as well as other possible ways to achieve these goals should be considered. In particular, other interventions may be needed for women who do not disclose or who do not receive support after disclosing. Interventions focussed on maintaining high levels of adherence in the absence of disclosure or support are needed for these women.

8.5.5 Stigma

As stigma occurs at the community level, and can also stem from structural and intersectional stigmas, reducing stigma will entail changing attitudes and beliefs at the community level. As stigma exists in multiple forms, it is recommended that interventions target specific dimensions [26], but gaps and challenges remain in developing effective interventions [84]. Ultimately, reducing stigma at the community level may lead to an environment that is more conducive of disclosure. As community-level stigma is beyond the scope of this thesis, the recommendations made here focus on the individual and service level.

As stated in Chapter 1, the Western Cape HIV treatment guidelines recommend that patients experiencing issues with non-disclosure or stigma should receive on-going counselling [85]. It is unclear how routinely and effectively this recommendation is implemented. A promising example of an individual-level intervention is peer support programmes to enhance individuals' ability to cope [86, 87]. As these programmes can be facilitated by lay health workers, they may be particularly feasible in LMIC settings. Given that stigma may have negative effects on HIV treatment outcomes through secrecy around HIV care engagement, strategies which limit the opportunities for inadvertent disclosure are needed. For example, differentiated models of care such as adherence clubs may enable women to avoid stigmatising situations by situating care outside of healthcare centres [88]. Considering the

fact that there will always be a proportion of women who do not disclose their HIV status, counselling messaging for these women should include concrete strategies for remaining engaged in care and maintaining high levels of adherence in the absence of disclosure.

8.5.6 Unintended pregnancy

As argued in Chapter 6 and earlier in this discussion, unintended pregnancy needs to be escalated as a global public health concern. Despite the prevention of unintended pregnancy constituting an important aspect of the World Health Organization's approach to prevent MTCT, most of the focus of global HIV prevention efforts have been on preventing MTCT to infants (prong 3) and, to a lesser extent, providing care and support to HIV-infected women and their children and families (prong 4) [89]. Indeed, the PMTCT cascade is conceptualised as beginning at HIV testing [90], and a much greater focus on preventing unintended pregnancies is warranted. Recommendations made here focus on (i) preventing unintended pregnancies and promoting safer pregnancies; and (ii) counselling in the context of an unintended pregnancy.

The health and social benefits of family planning are widely accepted [62]. Despite this, HIV care, maternal and child health services, and reproductive healthcare have historically existed as separate silos [91]. The argument for integrating family planning into HIV services has been repeatedly made [90, 92, 93]. Despite HIV treatment guidelines in the Western Cape recommending discussions of family planning with all patients on ART at every opportunity [85], healthcare providers do not routinely assess fertility goals in the country [94], and qualitative research suggests that the onus is on patients to initiate conversations about pregnancy intentions and contraception [95]. In the broader study from which these thesis data arose, one-quarter of women who were established on ART when entering antenatal care

reported not using contraceptives during the past 12 months [27]. Among women initiating ART during pregnancy in this cohort, high levels of contraceptive discontinuation alongside low desires for a future period were observed during the postpartum period [96]. Together, these data suggest a major gap for women who are engaged in routine HIV care and speak to the urgent need for an increased focus on family planning within health services.

Integrating family planning into HIV care services has been shown to be feasible [24] and effective [97]. Tools need to be developed and implemented to routinely screen for fertility intentions and contraceptive use [95]. Fertility intentions change over time [24] and should be assessed continuously, and implementation research will be critical to monitor implementation and understand how these recommendations can be achieved at scale [90]. Finally, integration must also include pre-conception care for individuals who intend to become pregnant [92]; indeed, reproductive health counselling must be tailored to reproductive goals [91]. In particular, the importance of viral suppression must be emphasised as part of pre-conception counselling [98, 99].

For women who are experiencing an unintended pregnancy, counselling messaging must acknowledge the heightened vulnerability that this confers. In addition, an unintended pregnancy occurs within complex social relationships and circumstances, as argued in various parts of this thesis, and counselling must take these broader issues into account. In particular, enhanced counselling should target women who are newly diagnosed HIV-positive in the context of an unintended pregnancy: in this context, women have little time to adjust to this two-fold impact on their lives [54]. Recommendations regarding counselling around disclosure for this group of women were made above. In addition, counselling messaging should target the effects of an unintended pregnancy on women's psychological well-being

and, as suggested by this thesis, long-term treatment outcomes. Indeed, women who did not intend to become pregnant may require ongoing support during the pregnancy and postpartum, alongside an enhanced focus on postpartum family planning in order to help prevent a repeat unintended pregnancy.

8.5.7 Understanding mechanisms

Finally, there is a need to investigate the mechanisms of the associations reported in this thesis and in the broader literature, as discussed above. Understanding causal mechanisms is critical to the design of interventions. This argument is best illustrated by considering HIV-related stigma: levels of stigma remain high globally, but an understanding of mechanisms could lead to interventions that block the pathway from stigma to the mediating variable, or from the mediator to the adverse outcome [26]. In this way, outcomes may improve even without reducing stigma at the community level. Similarly, levels of unintended pregnancy remain high globally, but no causal mechanism has been elucidated to date to explain observed associations between an unintended pregnancy and poor maternal and child outcomes [65]; an exploration of mediators could allow for targeted interventions. In the same line, a better understanding of potential effect modifiers is needed. Given that interventions to reduce each of stigma and unintended pregnancy appear to have had limited impact to date, understanding the factors that may buffer against negative outcomes is a critical next step in order to inform practice.

8.6 Conclusion

This thesis sought to provide insights into the patterns, predictors and impact of HIV-status disclosure among pregnant and postpartum women in the context of lifelong ART in South Africa, including considerations of stigma, social support, depression and unintended

pregnancy. Importantly, these analyses suggest that disclosure occurs as two separate processes in this sample of women: disclosure to a male partner, and disclosure to family/community members. The findings presented in this thesis provide strong evidence that women's social and economic circumstances are central to understandings of disclosure, mental health and HIV viral load. Indeed, both the prevalence of disclosure and its impact on depression and viral load were modified by women's circumstances. In this setting, disclosure does not appear to have universally beneficial effects on either depression or viral load; the effects do not appear to be consistent over time; and the effects differ according to women's relationships with the person(s) to whom they disclose. In these analyses, stigma emerged as a critical factor that adversely affects mental health, regardless of levels of social support. In addition, unintended pregnancy emerged as a critical factor that heightens women's vulnerability, both during the pregnancy and up to five years postpartum.

Massive progress has been made in preventing MTCT in South Africa and globally. Much of this progress has been due to population-wide public health approaches: routine HIV testing for all women as part of antenatal care; antiretroviral prophylaxis and now lifelong ART for all pregnant and breastfeeding women; and massive roll-outs of ART services within primary care settings throughout the country. Guidelines related to disclosure have similarly taken a blanket approach, with disclosure encouraged for its potential individual- and population-level benefits. This thesis provides compelling evidence that the individual cannot be ignored in research, policy or practice. Disclosure is a complex phenomenon that occurs within complicated social relationships, and there is a need for nuance in the promotion of disclosure; indeed, the individual must be made central in our approach to HIV prevention and care.

References

1. South African National Department of Health. The 2015 National Antenatal Sentinel HIV & Syphilis Survey Report. Pretoria: South African National Department of Health; 2017.
2. Bachanas P, Medley A, Pals S, Kidder D, Antelman G, Benech I, et al. Disclosure, knowledge of partner status, and condom use among HIV-positive patients attending clinical care in Tanzania, Kenya, and Namibia. AIDS Patient Care STDS. 2013;27(7):425-435.
3. Abdool Karim Q, Dellar RC, Bearnot B, Werner L, Frohlich JA, Kharsany ABM, et al. HIV-positive status disclosure in patients in care in rural South Africa: implications for scaling up treatment and prevention interventions. AIDS Behav. 2015;19:322-329.
4. Gadisa T, Tymejczyk O, Gorrell Kulkarni S, Hoffman S, Lahuerta M, Remien RH, et al. Disclosure history among persons initiating antiretroviral treatment at six HIV clinics in Oromia, Ethiopia, 2012-2013. AIDS Behav. 2017;21:70-81.
5. Hatcher AM, Turan JM, Leslie HH, Kanya LW, Kwena Z, Johnson MO, et al. Predictors of linkage to care following community-based HIV counseling and testing in rural Kenya. AIDS Behav. 2012;16:1295-1307.
6. Medley AM, Kennedy CE, Lunyolo S, Sweat MD. Disclosure outcomes, coping strategies, and life changes among women living with HIV in Uganda. Qual Health Res. 2009;19(12):1744-1754.
7. Groves AK, Maman S, Moodley D. HIV+ women's narratives of non-disclosure: resisting the label of immorality. Glob Public Health. 2012;7(8):799-811.
8. Bhatia DS, Harrison AD, Kubeka M, Milford C, Kaida A, Bajunirwe F, et al. The role of relationship dynamics and gender inequalities as barriers to HIV-serostatus disclosure: qualitative study among women and men living with HIV in Durban, South Africa. Front Public Health. 2017;5:188.
9. Kiweewa FM, Bakaki PM, McConnell MS, Musisi M, Namirembe C, Nakayiwa F, et al. A cross-sectional study of the magnitude, barriers, and outcomes of HIV status disclosure among women participating in a perinatal HIV transmission study, "the Nevirapine Repeat Pregnancy study". BMC Public Health. 2015;15:988.
10. Crankshaw TL, Voce A, Butler LM, Darbes L. Expanding the relationship context for couple-based HIV prevention: elucidating women's perspectives on non-traditional sexual partnerships. Soc Sci Med. 2016;166:169-176.
11. Medley A, Garcia-Moreno C, McGill S, Maman S. Rates, barriers and outcomes of HIV serostatus disclosure among women in developing countries: implications for prevention of mother-to-child transmission programmes. Bull World Health Organ. 2004;82(4):299-307.
12. Kiula ES, Damian DJ, Msuya SE. Predictors of HIV serostatus disclosure to partners among HIV-positive pregnant women in Morogoro, Tanzania. BMC Public Health. 2013;13:433.
13. Gillett HJ, Parr J. Disclosure among HIV-positive women: the role of HIV/AIDS support groups in rural Kenya. Afr J AIDS Res. 2010;9(4):337-344.
14. Flax VL, Yourkavitch J, Okello ES, Kadzandira J, Katahoire AR, Munthali AC. "If my husband leaves me, I will go home and suffer, so better cling to him and hide this

thing": the influence of gender on Option B+ prevention of mother-to-child transmission participation in Malawi and Uganda. PLoS ONE. 2017;12(6):e0178298.

15. Maeri I, El Ayadi A, Getahun M, Charlebois E, Akatukwasa C, Tumwebaze D, et al. "How can I tell?" Consequences of HIV status disclosure among couples in eastern African communities in the context of an ongoing HIV "test-and-treat" trial. AIDS Care. 2016;28(Suppl 3):59-66.
16. Duff P, Kipp W, Wild TC, Rubaale T, Okech-Ojony J. Barriers to accessing highly active antiretroviral therapy by HIV-positive women attending an antenatal clinic in a regional hospital in western Uganda. J Int AIDS Soc. 2010;13:37.
17. Norman A, Chopra M, Kadiyala S. Factors related to HIV disclosure in 2 South African communities. Am J Public Health. 2007;97:1775-1781.
18. Dorward J, Mabuto T, Charalambous S, Fielding KL, Hoffmann CJ. Factors associated with poor linkage to HIV care in South Africa: secondary analysis of data from the Thol'impilo trial. J Acquir Immune Defic Syndr. 2017;76:453-460.
19. dos Santos MML, Kruger P, Mellors SE, Wolvaardt G, van der Ryst E. An exploratory survey measuring stigma and discrimination experienced by people living with HIV/AIDS in South Africa: the People Living with HIV Stigma Index. BMC Public Health. 2014;14:80.
20. Hargreaves JR, Krishnaratne S, Mathema H, Lilleston PS, Sievwright K, Mandla N, et al. Individual and community-level risk factors for HIV stigma in 21 Zambian and South African communities: analysis of data from the HPTN071 (PopART) study. AIDS. 2018;32:783-793.
21. Nachega JB, Morroni C, Zuniga JM, Sherer R, Beyrer C, Solomon S, et al. HIV-related stigma, isolation, discrimination, and serostatus disclosure: a global survey of 2035 HIV-infected adults. J Int Assoc Physicians AIDS Care. 2012;11(3):172-178.
22. Stirratt MJ, Remien RH, Smith A, Copeland OQ, Dolezal C, Krieger D, et al. The role of HIV serostatus disclosure in antiretroviral medication adherence. AIDS Behav. 2006;10:483-493.
23. Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J, et al. A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women PLoS ONE. 2014;9(11):e111421.
24. Haberlen SA, Narasimhan M, Beres LK, Kennedy CE. Integration of family planning services into HIV care and treatment services: a systematic review. Stud Fam Plan. 2017;48(2):153-177.
25. Anglewicz P, Chintsanya J. Disclosure of HIV status between spouses in rural Malawi. AIDS Care. 2011;23(8):998-1005.
26. Turan B, Hatcher AM, Weiser SD, Johnson MO, Rice WS, Turan JM. Framing mechanisms linking HIV-related stigma, adherence to treatment, and health outcomes. Am J Public Health. 2017;107(6):863-869.
27. Iyun V, Brittain K, Phillips TK, le Roux S, Mcintyre JA, Zerbe A, et al. Prevalence and determinants of unplanned pregnancy in HIV-positive and HIV-negative pregnant women in Cape Town, South Africa: a cross-sectional study. BMJ Open. 2018;8:e019979.
28. Remien RH, Mellins CA. Long-term psychosocial challenges for people living with HIV: let's not forget the individual in our global response to the pandemic. AIDS. 2007;21(Suppl 5):S55-S63.

29. Chaudoir SR, Fisher JD. The Disclosure Processes Model: understanding disclosure decision making and postdisclosure outcomes among people living with a concealable stigmatized identity. Psychol Bull. 2010;136(2):236-256.
30. Chaudoir SR, Fisher JD, Simoni JM. Understanding HIV disclosure: a review and application of the Disclosure Processes Model. Soc Sci Med. 2011;72(10):1618-1629.
31. Visser MJ, Neufeld S, de Villiers A, Makin JD, Forsyth BWC. To tell or not to tell: South African women's disclosure of HIV status during pregnancy. AIDS Care. 2008;20(9):1138-1145.
32. Hunter-Adams J, Zerbe A, Philips T, Rini Z, Myer L, Petro G, et al. The dimensionality of disclosure of HIV status amongst post-partum women in Cape Town, South Africa. Afr J AIDS Res. 2017;16(2):101-107.
33. Obermeyer CM, Baijal P, Pegurri E. Facilitating HIV disclosure across diverse settings: a review. Am J Public Health. 2011;101(6):1011-1023.
34. Hult JR, Wrubel J, Bränström R, Acree M, Tedlie Moskowitz J. Disclosure and nondisclosure among people newly diagnosed with HIV: an analysis from a stress and coping perspective. AIDS Patient Care STDS. 2012;26(3):181-190.
35. Spangler SA, Abuogi LL, Akama E, Bukusi EA, Helova A, Musoke P, et al. From 'half-dead' to being 'free': resistance to HIV stigma, self-disclosure and support for PMTCT/HIV care among couples living with HIV in Kenya. Cult Health Sex. 2018;20(5):489-503.
36. Hardon A, Vernooij E, Bongololo-Mbera G, Cherutich P, Desclaux A, Kyaddondo D, et al. Women's views on consent, counseling and confidentiality in PMTCT: a mixed-methods study in four African countries. BMC Public Health. 2012;12:26.
37. Izudi J, Alioni S, Kerukadho E, Ndungutse D. Virological failure reduced with HIV-serostatus disclosure, extra baseline weight and rising CD4 cells among HIV-positive adults in northwestern Uganda. BMC Infect Dis. 2016;16:614.
38. Bajunirwe F, Arts EJ, Tisch DJ, King CH, Debanne SM, Sethi AK. Adherence and treatment response among HIV-1-infected adults receiving antiretroviral therapy in a rural government hospital in southwestern Uganda. J Int Assoc Physicians AIDS Care. 2009;8(2):139-147.
39. Lugalla J, Yoder S, Sigalla H, Madihi C. Social context of disclosing HIV test results in Tanzania. Cult Health Sex. 2012;14(Suppl 1):S53-S66.
40. Do NT, Phiri K, Bussmann H, Gaolathe T, Marlink RG, Wester CW. Psychosocial factors affecting medication adherence among HIV-1 infected adults receiving combination antiretroviral therapy (cART) in Botswana. AIDS Res Hum Retroviruses. 2010;26(6):685-691.
41. Ekama SO, Herbertson EC, Addeh EJ, Gab-Okafor CV, Onwujekwe DI, Tayo F, et al. Pattern and determinants of antiretroviral drug adherence among Nigerian pregnant women. J Pregnancy. 2012;2012:851810.
42. Yaya I, Landoh DE, Saka B, Patchali PM, Wasswa P, Aboubakari A-S, et al. Predictors of adherence to antiretroviral therapy among people living with HIV and AIDS at the regional hospital of Sokodé, Togo. BMC Public Health. 2014;14:1308.
43. Omonaiye O, Kusljic S, Nicholson P, Manias E. Medication adherence in pregnant women with human immunodeficiency virus receiving antiretroviral therapy in sub-Saharan Africa: a systematic review. BMC Public Health. 2018;18:805.
44. Albrecht S, Semrau K, Kasonde P, Sinkala M, Kankasa C, Vwalika C, et al. Predictors of nonadherence to single-dose nevirapine therapy for the prevention of

mother-to-child HIV transmission. J Acquir Immune Defic Syndr. 2006;41(1):114-118.

45. Varga CA, Sherman GG, Jones SA. HIV-disclosure in the context of vertical transmission: HIV-positive mothers in Johannesburg, South Africa. AIDS Care. 2005;18(8):952-960.
46. Maman S, Groves AK, McNaughton Reyes HL, Moodley D. Diagnosis and disclosure of HIV status: implications for women's risk of physical partner violence in the postpartum period. J Acquir Immune Defic Syndr. 2014;72:546-551.
47. Colombini M, Stöckl H, Watts C, Zimmerman C, Agamasu E, Mayhew SH. Factors affecting adherence to short-course ARV prophylaxis for preventing mother-to-child transmission of HIV in sub-Saharan Africa: a review and lessons for future elimination. AIDS Care. 2014;26(7):914-926.
48. Spangler SA, Onono M, Bukusi EA, Cohen CR, Turan JM. HIV-positive status disclosure and use of essential PMTCT and maternal health services in rural Kenya. J Acquir Immune Defic Syndr. 2014;67:S235-S242.
49. George MS, Lambert H. 'I am doing fine only because I have not told anyone': the necessity of concealment in the lives of people living with HIV in India. Cult Health Sex. 2015;17(8):933-946.
50. Rice E, Comulada S, Green S, Mayfield Arnold E, Rotheram-Borus MJ. Differential disclosure across social network ties among women living with HIV. AIDS Behav. 2009;13:1253-1261.
51. Busza J, Walker D, Hairston A, Gable A, Pitter C, Lee S, et al. Community-based approaches for prevention of mother to child transmission in resource-poor settings: a social ecological review. J Int AIDS Soc. 2012;15(Suppl 2):17373.
52. Miller ES, Yee LM, Dorman RM, McGregor DV, Sutton SH, Garcia PM, et al. Is maternal disclosure of HIV serostatus associated with a reduced risk of postpartum depression? Am J Obstet Gynecol. 2016;215:521.e1-5.
53. Jones TB. Psychosocial dimensions of HIV infection in pregnancy. Clin Obstet Gynecol. 2008;51(2):456-466.
54. Crankshaw TL, Voce A, King RL, Giddy J, Sheon NM, Butler LM. Double disclosure bind: complexities of communicating an HIV diagnosis in the context of unintended pregnancy in Durban, South Africa. AIDS Behav. 2014;18:S53-S59.
55. Smith R, Rossetto K, Peterson BL. A meta-analysis of disclosure of one's HIV-positive status, stigma and social support. AIDS Care. 2008;20(10):1266-1275.
56. McMahon SA, Kennedy CE, Winch PJ, Kombe M, Killewo J, Kilewo C. Stigma, facility constraints, and personal disbelief: why women disengage from HIV care during and after pregnancy in Morogoro region, Tanzania. AIDS Behav. 2017;21:317-329.
57. Sweeney SM, Vanable PA. The association of HIV-related stigma to HIV medication adherence: a systematic review and synthesis of the literature. AIDS Behav. 2016;20:29-50.
58. Katz IT, Ryu AE, Onuegbu AG, Psaros C, Weiser SD, Bangsberg DR, et al. Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis. J Int AIDS Soc. 2013;16(Suppl 2):18640.
59. Phelan S. Pregnancy: a "teachable moment" for weight control and obesity prevention. Am J Obstet Gynecol. 2010;202:135.e1-8.

60. McBride CM, Puleo E, Pollak KI, Clipp EC, Woolford S, Emmons KM. Understanding the role of cancer worry in creating a "teachable moment" for multiple risk factor reduction. Soc Sci Med. 2008;66:790-800.
61. Clouse K, Schwartz S, Van Rie A, Bassett J, Yende N, Pettifor A. "What they wanted was to give birth; nothing else": barriers to retention in Option B+ HIV care among postpartum women in South Africa. J Acquir Immune Defic Syndr. 2014;67:e12-e8.
62. Tsui AO, McDonald-Mosley R, Burke AE. Family planning and the burden of unintended pregnancies. Epidemiol Rev. 2010;32:152-174.
63. Feyissa TR, Harris ML, Melka AS, Loxton D. Unintended pregnancy in women living with HIV in sub-Saharan Africa: a systematic review and meta-analysis. AIDS Behav. 2018: Epub ahead of print.
64. Peltzer K, Rodriguez VJ, Jones D. Prevalence of prenatal depression and associated factors among HIV-positive women in primary care in Mpumalanga province, South Africa. SAHARA J. 2016;13(1):60-67.
65. Lewinsohn R, Crankshaw T, Tomlinson M, Gibbs A, Butler L, Smit J. "This baby came up and then he said, "I give up!": The interplay between unintended pregnancy, sexual partnership dynamics and social support and the impact on women's well-being in KwaZulu-Natal, South Africa. Midwifery. 2018;62:29-35.
66. Dima AL, Stutterheim SE, Lyimo R, de Bruin M. Advancing methodology in the study of HIV status disclosure: the importance of considering disclosure target and intent. Soc Sci Med. 2014;108:166-174.
67. Préau M, Beaulieu-Prévost D, Henry E, Bernier A, Veillette-Bourbeau L, Otis J. HIV serostatus disclosure: development and validation of indicators considering target and modality. Results from a community-based research in 5 countries. Soc Sci Med. 2015;146:137-146.
68. Ssali SN, Atuyambe L, Tumwine C, Segujja E, Nekesa N, Nannungi A, et al. Reasons for disclosure of HIV status by people living with HIV/AIDS and in HIV care in Uganda: an exploratory study. AIDS Patient Care STDS. 2010;24(10):675-681.
69. Hatcher AM, Stöckl H, Christofides N, Woollett N, Pallitto CC, Garcia-Moreno C, et al. Mechanisms linking intimate partner violence and prevention of mother-to-child transmission of HIV: a qualitative study in South Africa. Soc Sci Med. 2016;168:130-139.
70. Bernstein M, Phillips T, Zerbe A, McIntyre JA, Brittain K, Petro G, et al. Intimate partner violence experienced by HIV-infected pregnant women in South Africa: a cross-sectional study. BMJ Open. 2016;6:e011999.
71. Kennedy CE, Haberlen S, Amin A, Baggaley R, Narasimhan M. Safer disclosure of HIV serostatus for women living with HIV who experience or fear violence: a systematic review. J Int AIDS Soc. 2015;18(Suppl 5):20292.
72. Conserve DF, Groves AK, Maman S. Effectiveness of interventions promoting HIV serostatus disclosure to sexual partners: a systematic review. AIDS Behav. 2015;19:1763-1772.
73. Roxby AC, Matemo D, Drake AL, Kinuthia J, John-Stewart GC, Ongecha-Owuor F, et al. Pregnant women and disclosure to sexual partners after testing HIV-1-seropositive during antenatal care. AIDS Patient Care STDS. 2013;27(1):33-37.
74. Vu L, Andrinopoulos K, Mathews C, Chopra M, Kendall C, Eisele TP. Disclosure of HIV status to sex partners among HIV-infected men and women in Cape Town, South Africa. AIDS Behav. 2012;16:132-138.

75. Hawkins D, Blott M, Clayden P, de Ruiter A, Foster G, Gilling-Smith C, et al. Guidelines for the management of HIV infection in pregnant women and the prevention of mother-to-child transmission of HIV. HIV Med. 2005;6(Suppl 2):107-148.
76. Bott S, Obermeyer CM. The social and gender context of HIV disclosure in sub-Saharan Africa: a review of policies and practices. SAHARA J. 2013;10(Suppl 1):S5-S16.
77. Préau M, Laguette V, March L, Rabaud C, Hardel L, Protopopescu C, et al. Discussing HIV status: is it easier after 10 years of antiretroviral treatment? The ANRS CO8 APROCO-COPILOTE Cohort. AIDS Behav. 2017;21:118-128.
78. Kennedy CE, Fonner VA, Armstrong KA, O'Reilly KR, Sweat MD. Increasing HIV serostatus disclosure in low and middle-income countries: a systematic review of intervention evaluations. AIDS. 2015;29(Suppl 1):S7-S23.
79. Colombini M, James C, Ndwiga C, Integra team, Mayhew SH. The risks of partner violence following HIV status disclosure, and health service responses: narratives of women attending reproductive health services in Kenya. J Int AIDS Soc. 2016;19(1):20766.
80. Walcott MM, Hatcher AM, Kwena Z, Turan JM. Facilitating HIV status disclosure for pregnant women and partners in rural Kenya: a qualitative study. BMC Public Health. 2013;13:1115.
81. Sherr L, Croome N. Involving fathers in prevention of mother to child transmission initiatives - what the evidence suggests. J Int AIDS Soc. 2012;15(Suppl 2):17378.
82. Desgrées-du-Loû A, Orne-Gliemann J. Couple-centred testing and counselling for HIV serodiscordant heterosexual couples in sub-Saharan Africa. Reprod Health Matters. 2008;16(32):151-161.
83. Bärnighausen T, Chaiyachati K, Chimbindi N, Peoples A, Haberer J, Newell M-L. Interventions to increase antiretroviral adherence in sub-Saharan Africa: a systematic review of evaluation studies. Lancet Infect Dis. 2011;11:942-951.
84. Stangl A, Lloyd JK, Brady LM, Holland CE, Baral S. A systematic review of interventions to reduce HIV-related stigma and discrimination from 2002 to 2013: how far have we come? J Int AIDS Soc. 2013;16(3 Suppl 2):18734.
85. Western Cape Department of Health. The Western Cape consolidated guidelines for HIV treatment: prevention of mother-to-child transmission of HIV (PMTCT), children, adolescents and adults. Cape Town: Western Cape Department of Health; 2018.
86. Beres LK, Narasimhan M, Robinson J, Welbourn A, Kennedy CE. Non-specialist psychosocial interventions for women living with HIV: a systematic review. AIDS Care. 2017;29(9):1079-1087.
87. Mundell JP, Visser MJ, Makin JD, Forsyth BW, Sikkema KJ. Support group processes: perspectives from HIV-infected women in South Africa. Qual Res Psychol. 2012;9(2):173-187.
88. Trafford Z, Gomba Y, Colvin CJ, Iyun VO, Phillips TK, Brittain K, et al. Experiences of HIV-positive postpartum women and health workers involved with community-based antiretroviral therapy adherence clubs in Cape Town, South Africa. BMC Public Health. 2018;18:935.
89. Crankshaw TL, Smit JA, Beksinska ME. Placing contraception at the centre of the HIV prevention agenda. Afr J AIDS Res. 2016;15(2):157-162.

90. Wilcher R, Petruney T, Cates W. The role of family planning in elimination of new pediatric HIV infection. Curr Opin HIV AIDS. 2013;8(5):490-497.
91. Mantell JE, Exner TM, Cooper D, Bai D, Leu C-S, Hoffman S, et al. Pregnancy intent among a sample of recently diagnosed HIV-positive women and men practicing unprotected sex in Cape Town, South Africa. J Acquir Immune Defic Syndr. 2014;67:S202-S209.
92. Rahangdale L, Stewart A, Stewart RD, Badell M, Levison J, Ellis P, et al. Pregnancy intentions among women living with HIV in the United States. J Acquir Immune Defic Syndr. 2014;65:306-311.
93. Sutton MY, Patel R, Frazier EL. Unplanned pregnancies among HIV-infected women in care - United States. J Acquir Immune Defic Syndr. 2014;65:350-358.
94. Matthews LT, Milford C, Kaida A, Ehrlich MJ, Ng C, Greener R, et al. Lost opportunities to reduce periconception HIV transmission: safer conception counseling by South African providers addresses perinatal but not sexual HIV transmission. J Acquir Immune Defic Syndr. 2014;67:S210-S217.
95. West N, Schwartz S, Phofa R, Yende N, Bassett J, Sanne I, et al. "I don't know if this is right ... but this is what I'm offering": healthcare provider knowledge, practice, and attitudes towards safer conception for HIV-affected couples in the context of Southern African guidelines. AIDS Care. 2016;28(3):390-396.
96. Towriss CA, Phillips TK, Brittain K, Zerbe A, Abrams EJ, Myer L. The injection or the injection? Restricted contraceptive choices among women living with HIV. Sex Reprod Health Matters. 2019;27(1):1628593.
97. Gay J, Hardee K, Croce-Galis M, Hall C. What works to meet the sexual and reproductive health needs of women living with HIV/AIDS. J Int AIDS Soc. 2011;14:56.
98. Steiner RJ, Black V, Rees H, Schwartz SR. Low receipt and uptake of safer conception messages in routine HIV care: findings from a prospective cohort of women living with HIV in South Africa. J Acquir Immune Defic Syndr. 2016;72:105-113.
99. Brittain K, Remien RH, Mellins CA, Phillips TK, Zerbe A, Abrams EJ, et al. Determinants of suboptimal adherence and elevated HIV viral load in pregnant women already on antiretroviral therapy when entering antenatal care in Cape Town, South Africa. AIDS Care. 2018:30(12):1517-1523.

Appendix 1: Schedule of study measurements in the MCH-ART study

	Phase 1 *(all HIV+ pregnant women)*	**Phase 2** *(HIV+ pregnant women eligible for ART)*			**Phase 3** *(HIV+ postpartum women on ART and breastfeeding)*				
Item for completion	**1st antenatal visit (study visit 1)**	**2nd antenatal visit (study visit 2)**	**Late 3rd trimester (study visit 3)**	**< 7 days pp (up to 28 days) (study visit 4)**	**6 weeks pp (study visit 5)**	**3 months pp (study visit 6)**	**6 months pp (study visit 7)**	**9 months pp (study visit 8)**	**12 months pp (study visit 9)**
Procedural forms									
Eligibility Checklist	X	X		X					
Informed Consent	#1	#2		#3					
Locator Information [1]	X	X	X	X	X	X	X	X	
Randomization Log				X					
Questionnaires									
Demographics & medical history	X	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]
HIV Knowledge Inventory	X[2]	X			X			X	
Treatment Knowledge Inventory	X[2]	X			X			X	
ART Medication Beliefs	X[2]	X			X			X	
Adherence self-efficacy	X[2]	X	X				X		X
K-10 & EPDS [4]		X			X				X
Alcohol/substance use screen [5]		X	X				X		X
Trauma/abuse assessment		X		X					X
Social impact scale		X			X				X
Availability of social support scale		X	X				X		X
Infant feeding intentions/practices			X	X	X	X	X	X	X
Family planning use/intentions	X			X	X		X	X	X
Pregnancy intentions	X			X	X		X	X	X
Patient-Provider relationship scale			X	X	X		X	X	X
Unplanned Pregnancy assessment	X								
Maternal adherence [6]	X[2]	X	X	X	X	X	X	X	X
Infant adherence[6]				X	X				

	Phase 1 *(all HIV+ pregnant women)*	**Phase 2** *(HIV+ pregnant women eligible for ART)*			**Phase 3** *(HIV+ postpartum women on ART and breastfeeding)*				
Item for completion	**1st antenatal visit (study visit 1)**	**2nd antenatal visit (study visit 2)**	**Late 3rd trimester (study visit 3)**	**< 7 days pp (up to 28 days) (study visit 4)**	**6 weeks pp (study visit 5)**	**3 months pp (study visit 6)**	**6 months pp (study visit 7)**	**9 months pp (study visit 8)**	**12 months pp (study visit 9)**
Child Grants					X		X		X
Anthropometry									
Maternal anthropometry [7]					X	X	X	X	X
Infant growth parameters					X	X	X	X	X
Study laboratory measures									
HIV viral load	X	X	X	X	X	X	X	X	X
Maternal stored serum	X	X	X	X	X		X	X	X
Infant HIV PCR testing									X
Infant rapid antibody test									X
Clinical data abstraction [8]									
ART initiation & follow-up		X	X	X	X	X	X		X
Antenatal & obstetric information	X	X	X	X					
Pharmacy ART dispensing records		X	X	X	X	X	X	X	X
Maternal laboratory test results [9]	X	X					X		X
Infant growth and well-being				X	X	X	X	X	X
Infant HIV PCR result [9]					X		X		

1. Participants' locator information will be updated at each study visit, if it has changed since the last visit.
2. These assessments will be administered to participants who are already on ART at the time of enrolment into Phase 1.
3. A subset of demographic questions will be asked at all antenatal and postnatal study visits.
4. Kessler-10 (screening questionnaire for non-specific psychological distress) and Edinburgh Postnatal Depression Survey.
5. Alcohol use disorders identification test (AUDIT) and drug use disorders identification test (DUDIT).
6. Adherence assessments will include maternal ART adherence and, postpartum, questions related to infant adherence nevirapine prophylaxis and co-trimoxazole.
7. Note that maternal weight & mid-upper arm circumference will be measured at each Phase 3 study visit; maternal height will only be measured at the 6 week postpartum visit
8. Abstraction of routine clinical data and laboratory data will take place at the end of the study.
9. Results of routine laboratory testing on mothers (including pre-ART and on-ART CD4 cell count, pre-ART serum creatinine, alanine aminotransferase and full blood count) and infants (HIV PCR at 6 weeks and 2 weeks after cessation of breastfeeding; here marked for the 6 month visit) will come from record review.

Appendix 2: Study measures at the 36-60 month postpartum study visit

36-60 month visit	
Procedural forms	**Study laboratory measures**
Informed Consent for LACE study visit	HIV viral load
Informed consent for genetic testing	HIV resistance testing
Locator Information	Genotyping
Questionnaires	Drug resistance testing (TDF/EFV)
Demographics & medical history	Maternal stored plasma
Movement	
K-10 & EPDS	**Clinical data abstraction**
Alcohol/substance use screen	Antenatal and PMTCT information for subsequent pregnancies
Trauma/abuse assessment	ART initiation and follow-up data
Social impact scale	Pediatric information
Availability of social support scale	**Anthropometry**
Child questionnaire	Maternal anthropometry
Family planning use & Pregnancy Intentions	Child anthropometry
Patient-Provider relationship scale	
Maternal ART adherence & side effects	**Child development**
Child Grants	Ages & Stages ASQ-3
	Ages & Stages ASQ:SE-2
Food security	
Life events	
Adverse childhood experiences	
Partner questionnaire	